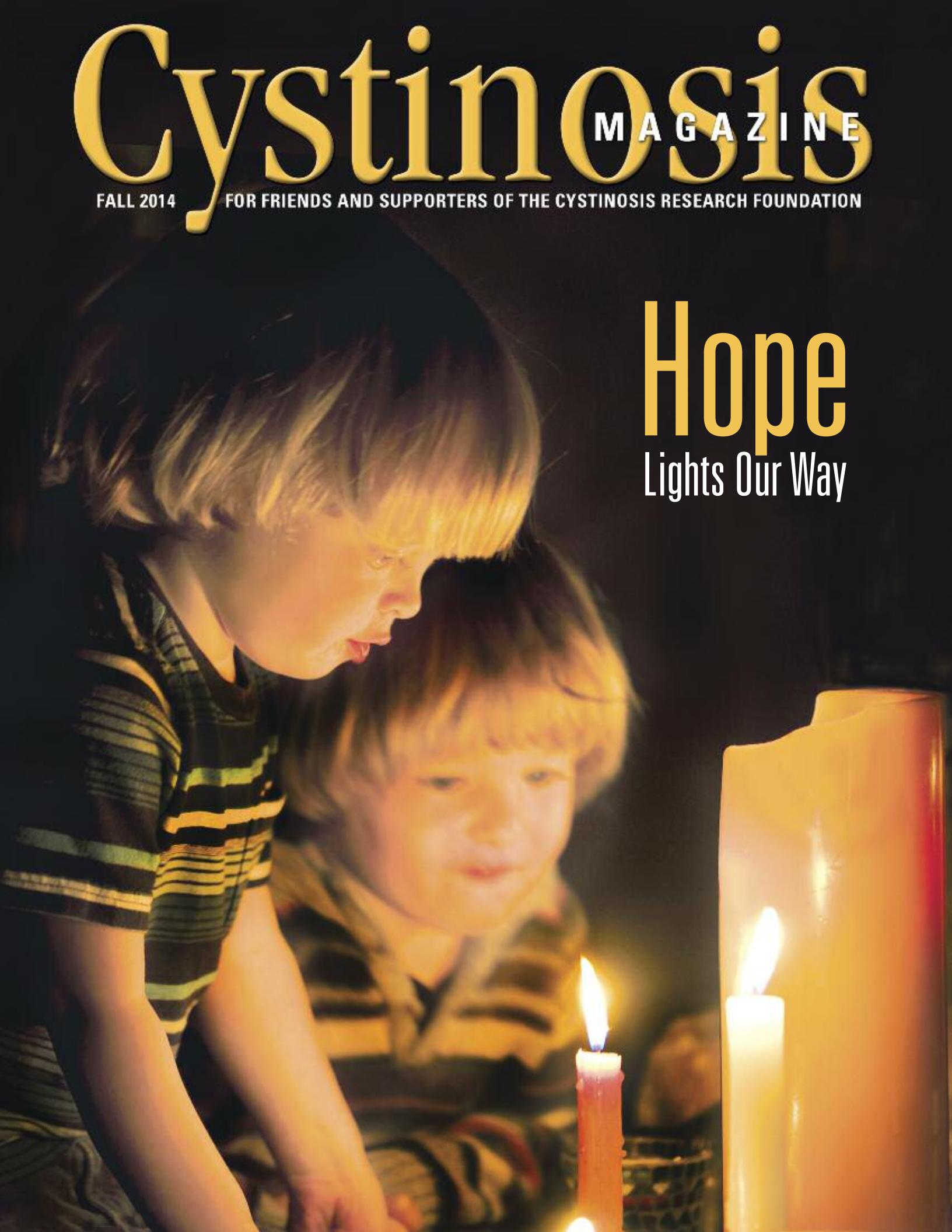
Cystinosis MAGAZINE

FALL 2014 FOR FRIENDS AND SUPPORTERS OF THE CYSTINOSIS RESEARCH FOUNDATION



Hope
Lights Our Way

Cystinosis is a rare, inherited, metabolic disease that is characterized by the abnormal accumulation of the amino acid cystine in each of the body's cells. Build-up of cystine in the cells eventually destroys all major organs of the body including the kidneys, liver, eyes, muscles, bone marrow, thyroid and brain.

CYSTINOSIS RESEARCH FOUNDATION

RESEARCH • HOPE • CURE

Medication is available to control some of the symptoms of this terrible disease, but cystinosis remains incurable.

Cystinosis affects approximately 500 people, mostly children, in North America and fewer than 2,000 worldwide. It is one of the 7,000 rare or "orphan" diseases in the United States that collectively impacts approximately 30 million Americans.

Federal funding for research on cystinosis and other rare diseases is virtually non-existent and most pharmaceutical companies remain uninterested because financial rewards are too small. Yet, while there is only a small number of patients who suffer from any given "orphan" disease, knowledge gained by studying one disease often leads to advancements in other rare diseases and more prevalent and well-known disorders.

Currently, there is no cure for cystinosis but there is *hope.*

The Cystinosis Research Foundation was established in 2003 with the sole purpose of raising funds to find better treatments and ultimately a cure for cystinosis.

Today, CRF is the largest provider of grants for cystinosis research in the world, funding more than 122 studies in 12 countries. CRF has raised $25.8 million, which it has granted or committed to cystinosis research studies around the world. CRF's efforts have changed the course of cystinosis research and given new energy to its investigators and scientists. CRF's commitment to research has given hope and promise to the global community of cystinosis patients and their families.

CYSTINOSISRESEARCH.ORG
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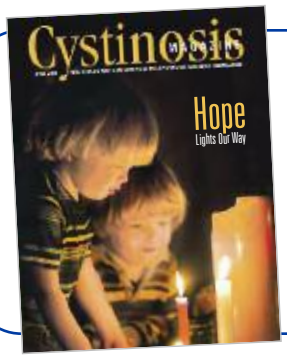

On the cover:
Seth and Leif, two-year-old twins from Calgary, Canada. The photo was taken by their father Nathan deBruyn.

Please send your suggestions and comments regarding *Cystinosis Magazine* to nstack@cystinosisresearch.org.

To receive our e-newsletter, *Star Facts*, send your email address to zsolsby@cystinosisresearch.org.

The entire cost of *Cystinosis Magazine* is underwritten by friends of the Cystinosis Research Foundation.

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THE Circle OF Hope

Dear Friends and Family:

The breathtaking cover image is of Seth and Leif, two-year-old twins from Calgary, Canada. They are the children of Kristen Murray and Nathan deBruyn who marked the anniversary of Seth's diagnosis with cystinosis by asking their friends and family to light a candle in Seth's honor. The candle symbolizes hope and light, and the gratitude they feel for their family and community who have embraced them as they travel this new journey with cystinosis. I know you will be moved by the touching article written by Kristen on page 6.

From the dark days of a cystinosis diagnosis to the new "normal" routine of life with cystinosis, we find light as a community. When life seemed impossibly dark and hopeless, we found inspiration from our children; their resilience and courage, and joy of living brought us light and fueled our determination to find a cure for cystinosis.

Simply put, we would not have the hope we have in abundance today without our researchers and scientists who have dedicated their lives to finding a cure for our children. Without research, there is no reason to believe that better treatments and a cure would be found. CRF is the only foundation in the world funding millions of dollars in new research every year. CRF is the lifeline that keeps the cycle of cystinosis research dynamic and thriving.

A BANNER YEAR FOR FUNDING RESEARCH!

This has been an outstanding year for CRF – to date we have funded more than $1.5 million in new grants. We have over $1 million available for new grants, which will be announced in December. We are grateful to our world-renowned CRF Scientific Review Board members who critically evaluate and then recommend the best proposals for funding. We continue to fund only the brightest and most committed researchers who promise to find better treatments and a cure. We are excited to fund researchers whose work will translate to clinical trials and we are dedicated to funding researchers who make discoveries about cystinosis that help us understand the disease and aid those seeking cures.

We have made tremendous progress, yet cystinosis remains an incurable, progressive disease – we are close to the cure, but we are not there yet.

Since 2003, the year Natalie made her birthday wish, ***to have my disease go away forever***, and the year the foundation was established, CRF has funded 122 research grants in 12 counties. CRF-funded researchers have published over 50 articles in prestigious journals. Because of your support, we have funded researchers whose work has exponentially increased the breadth and knowledge about cystinosis and as a result of that knowledge, new discoveries have been made about the pathogenesis of cystinosis.

A few of the research highlights resulting from CRF funding:

New FDA-approved Drug in 2013 – The delayed-release form of cysteamine is the life-saving drug for our children. The original medication must be taken every six hours of everyday but the delayed-release medication is taken every 12 hours. The delayed-release medication has significantly improved the quality of life, reduced side effects, and has allowed patients to sleep through the night.

Stem Cell and Gene Therapy Study – Dr. Stéphanie Cherqui at the University of California, San Diego, continues to make significant progress with the stem cell and gene therapy study and is working on pre-clinical toxicology studies. She recently formed the *Cystinosis Stem Cell and Gene Therapy Consortium.* The consortium includes experts in the fields of nephrology, neurology, endocrinology, gastroenterology, ophthalmology, bone marrow transplantation and gene therapy, and members of the cystinosis community. Consortium members will work on the design of the clinical trial for autologous stem cell transplantation. There is no doubt that Dr. Cherqui will lead us to the cure. (See article on page 27.)

Nanowafer Project for Corneal Cystinosis – CRF is funding the work of Dr. Ghanshyam Acharya at the Baylor College of Medicine and Dr. Jennifer Simpson at University of California, Irvine, and is working closely with them on developing a clinical trial to test a novel treatment for corneal cystinosis. We will begin work with the FDA to comply with their requirements and move towards a clinical trial in late 2015 or early 2016.

Cystinosis Research Helps Other Diseases and Disorders – One of the most fulfilling and unexpected results of funding cystinosis research is that it has resulted in new potential treatments for other diseases and disorders, including Huntington's disease, Parkinson's disease, NASH (fatty liver disease) and other systemic diseases similar to cystinosis.

In fact, in a recent article by Dr. Cherqui published July, 2014 in *Stem Cells* the article states that the work is, "*The first report of correction of a genetic lysosomal defect by bidirectional vesicular exchange via TNTs and suggests broader potential for HSC transplantation for other disorders due to defective vesicular proteins.*" In lay terms, her discoveries with stem cells have potential to help other diseases including other kidney diseases. This is extraordinary!

Your support of cystinosis research has extended far beyond the cystinosis community in ways that we could never have anticipated.

THE CYSTINOSIS COMMUNITY AND HOPE

Cystinosis is a rare metabolic disease that affects every cell in the body. It eventually destroys every organ in the body including the liver, kidneys, eyes, muscles, thyroid and brain. On average our children take between 8–12 medications every day. Life with cystinosis is not easy. As our children live into adulthood, more complications occur including muscle wasting, difficulty swallowing, neurological issues and for some, blindness. The medications our children take cause constant discomfort and pain – cystinosis is a relentless disease.

Almost every week I talk to a parent or caregiver or patient who shares their story about their life with cystinosis. Most stories are heartbreaking. Last week I heard from a family whose little girl was just diagnosed – she is three-and-a-half years old and is the size of a two-year-old because of years of misdiagnosis. She had not started the medications yet but had blessedly found a doctor (three hours away!) who knew something about cystinosis. Their story was heartwrenching because their child is so ill, but they were thankful to finally have a diagnosis. The family is now part of the CRF family and has the support and resources of our community. We can give them the greatest gift of all – hope! Their child has a brighter future because CRF researchers are working every minute of every day to find a cure.

I hear the stories of the small children with cystinosis and I am reminded that we lived through similar days with Natalie. Natalie still lives a life filled with doctor's appointments, hospitalizations, blood draws, severe gastrointestinal side effects, medical procedures and medications.

Thank you for shining your light on us – thank you for giving us the greatest gift of all – Hope.

Years ago, as we came to terms with cystinosis, we, like all other families with cystinosis, found our new "normal," we found "light" in darkness, and we found hope instead of despair. We rediscovered laughter, joy and we celebrated every healthy day. And through the eyes of our children, we learned to embrace life.

Natalie is living an independent life and is forging ahead with her master's degree! Twenty-three years ago, we were told that Natalie would not live to graduate from high school – those doctors did not know about the power of determined parents and a resilient child! They did not know that all of you would join us in the quest to cure cystinosis!

Cystinosis is a progressive disease and until **we find the cure,** there is no cure but our faith is strong and our determination steadfast. We must work until we find a cure for our children.

Each and every one of you has supported us on this life journey and we are forever thankful and grateful for your love and unwavering commitment. Your support and prayers have lifted us up and given us the strength we need to continue the quest for the cure.

We have accomplished extraordinary goals and we are within reach of new treatments that will change the course of cystinosis. With your support, we will continue to fund the best and the brightest researchers in the world who will undoubtedly lead us to the cure.

Thank you for supporting cystinosis research, for standing by our side and letting us lean on you when the days were dark. Thank you for shining your light on us – thank you for giving us the greatest gift of all – HOPE.

With heartfelt thanks,

Nancy and Jeff

A NOTE FROM NATALIE

Dear Friends and Family:

I started graduate school this fall at the University of Southern California. I am thrilled to be a student at USC, since it has always been my dream school. The Social Work program is definitely keeping me busy! There are a lot of papers and exams, but I am learning a great deal at the same time. I am taking five classes and interning at JAHI Family Service.

JAHI focuses on family preservation and protecting children. I am interested in working with children, so my experience at the agency has really expanded my interests and knowledge of social work. I feel very fortunate to be able to attend USC and have the opportunity to make a difference in the world.

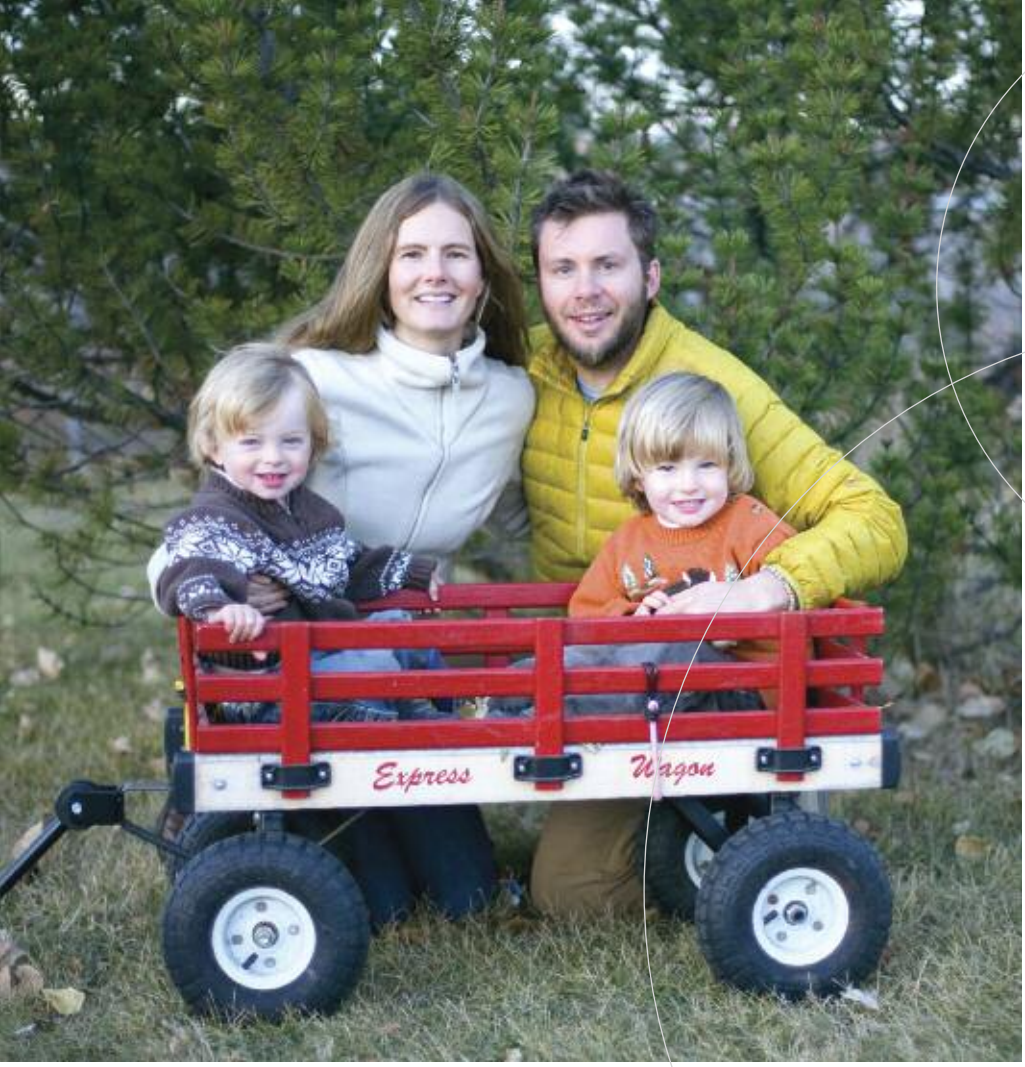
Since starting the program at USC, I have reflected on the cystinosis community and become more appreciative of its role in helping others. The love and support within our community has given the families and children affected by this disease hope and strength. I have learned that our strengths outweigh our weaknesses on the whole; we are a compassionate, dedicated and resilient group of people who have had to and continue to overcome many obstacles that most others do not face in their lives. We do not see cystinosis as a burden, but as a chance to live life to the fullest without any regrets. Our optimism and enthusiasm allows each of us to live positive lives.

I am so thankful to everyone who has supported us through the years. The dedication we have to finding a cure is remarkable and I am certain that one day my wish **– to have my disease go away forever –** will come true.

Love, Natalie

Photo above: Natalie surrounded by her many friends, most of whom are also cystinosis patients, at the CRF Day of Hope Family Conference in April 2014.

We do not see cystinosis as a burden, but as a chance to live life to the fullest without any regrets.



By Kristen Murray and Nathan deBruyn
Seth and Leif's mom and dad
Calgary, Canada

By the time you read this article, Seth deBruyn's Circle of Hope event will have taken place. The event, so beautifully explained in Kristen's recent letter to family members and friends is a touching and powerful reminder to each of us that we must never give up hope.

Kristen's letter also reminds us that we have come a long way and that we have much to be thankful for. But we still need your financial support on our journey to the cure.

Seth's Circle of

Dear friends,

On the evening of October 21, 2013, we were just finishing dinner when the phone rang. Nathan left the table to take the call and returned with a look of shock and confusion. With a quiet voice, he shared that Seth had been diagnosed with cystinosis, a metabolic disorder that causes an abnormal accumulation of cystine in the cells. In its early stages, cystinosis causes damage to the kidneys and eyes, and if left untreated it can compromise all organs and tissues in the body, including the muscles, thyroid, pancreas, liver and brain.

The hours that followed the phone call were very dark and we were overcome with feelings of grief. We were devastated to learn that our beloved son had a rare and potentially debilitating disease – one that is confirmed in fewer than 2,000 people worldwide, most of them children and young adults. As the days passed, we slowly came to terms with the "new journey" we had begun – and with what would be our new sense of "normal."

We learned how to administer the myriad medications Seth must take every six hours around the clock; talked to experts in the field; connected with other families impacted by cystinosis; and reached out to you, our family and friends. With this, the darkness that had encroached upon us relented and light slowly filtered in with each forward step that we took.

As we approach the year anniversary of Seth's diagnosis, lightness has replaced the dark and there is much to be grateful for. Seth has been amazingly strong and courageous in the face of adversity. He takes 18 doses of awful tasting medication or "vitamins" each day with little resistance, sometimes even saying, "Thank you," after we wake him to administer his 1:30 a.m. dose. Though Seth's medication often causes him to have a sore tummy, it is helping to mitigate cystine accumulation in his cells and to stabilize his electrolytes. With this, his growth is back on the charts. He is making excellent gains in both weight and height, and he is developing beautifully.

At two-and-a-half years old, Seth and his twin brother Leif have developed a profound bond with one another, fully embracing life as they run, ride bikes, build sand castles, pick tomatoes in our garden and engage with curiosity and fascination as they explore the world side by side. Their individual personalities are shining through more and more each day as they are speaking in full (well, almost full!) sentences. One of Leif's favorites is, "Where Seshy goes?" if Seth is not immediately by his side, and, "Focus, Seshy," if Seth is distracted while

taking his "vitamins." As Leif expresses himself as a responsible and caring "older" brother (if only by two minutes), Seth is emerging as an intuitive and compassionate soul. Upon entering a room, he has been known to ask, "How everyone doing here?" and when Leif is hurt or sad, Seth offers him a hug, and, looking intently at him, asks, "Feel better now?"

Beyond the present, we also have so much to be hopeful for in the years to come. There is currently no cure for cystinosis, but research supported by the Cystinosis Research Foundation (CRF) shows great promise. CRF researchers are currently preparing for human trials using autologous stem cell therapy to reverse cystinosis. It is clear that a cure is on the horizon and that a life free of cystinosis is a very real prospect for Seth … and all children affected by the disease.

If you are planning to give to charity this year, we ask you to support CRF in Seth's honor. (See sidebar at left) CRF offers those with cystinosis a reason to be hopeful. The foundation is entirely funded by family and friends of those with the disease. With all donations going directly to support research, every dollar makes a difference.

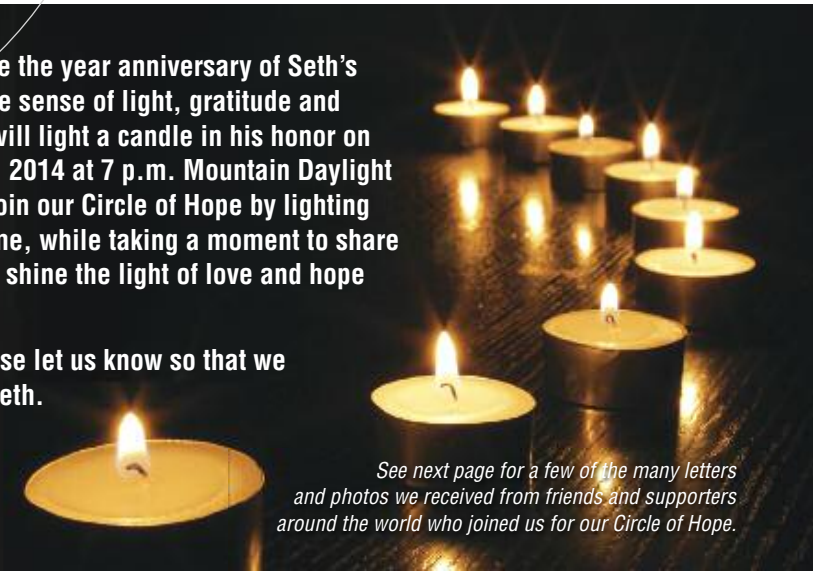
With love and appreciation, Kristen, Nathan, Leif and Seth

We reflected on the renewed sense of gratitude we feel in an article that was published in the summer issue of *Cystinosis Magazine.* You can find the article on page 30 of the link below: www.cystinosisresearch.org/wp-content/uploads/2014/07/CRF_Magazine_2014_Spring_Summer_Edition.pdf

To commemorate the year anniversary of Seth's diagnosis with the sense of light, gratitude and hope we feel, we will light a candle in his honor on Tuesday, October 21, 2014 at 7 p.m. Mountain Daylight Time. We invite you to join our Circle of Hope by lighting your own candle at the same time, while taking a moment to share in our gratitude for the many blessings in our lives – and to shine the light of love and hope on Seth and all children living with cystinosis.

If you plan to join us from afar on Tuesday October 21, please let us know so that we can hold you in our thoughts as we light a candle for Seth.

Hope



See next page for a few of the many letters and photos we received from friends and supporters around the world who joined us for our Circle of Hope.

We received an extraordinary response to the letter we sent out (see previous page) and we were moved by the compassion and kindness that people extended and the interest that they expressed in joining our Circle of Hope. As our friends and family sent our message to their friends and extended families, our circle grew exponentially. Together with hundreds of people from across Canada and the world, we lit our candles at 7 p.m. on October 21. We reflected on the year that had passed since Seth's diagnosis and felt deep gratitude for the love and hope that surrounds us. Here are a few of the messages we received:

Hi Kristen,

What a journey you are on. Thank you for sharing it with us. I sent the list and cc'd you because I wanted you to know that you have touched so many. I received one note from my friend who will be at a board meeting tonight and asked if it would be ok if she shares this with the board. Even though you are the one living each moment through this, there are many cheering you on. Tonight at 7 my family will light a candle for your family, for Seth, and the others facing similar challenges.

Sending you lots of energy and love,

Ann (Ann Gray-Elton)
Calgary, Canada

To friends in Calgary and beyond:

I am forwarding this email from my friend and former colleague Kristen Murray. Her story – actually the story of her son and their family's hope and determination and gratefulness is inspiring.

Kristen is asking for support through a Circle of Hope on Tuesday night at 7 MST. If you can think of them and send prayers and positive energy especially at that time, that would be wonderful. If you want to make a donation, there is info about that at the bottom of her note too.

Kristen had first shared this information in her Christmas note when she told of Seth's condition as though written from his twin brother's perspective. Dealing with adversity can bring out strengths that we never know about any other way. This is one such sharing that has inspired me to want to pass it on.

Have a great day.

Ann (Ann Gray-Elton)
Calgary, Canada

Dear Kristen and Nathan,

We decided to light our Candle of Hope in the living room where Seth and Leif enjoyed playing during your last visit. The candle stood beside a photo of Seth in the little blue life jacket he wore while we played at the beach last summer. As Grandpa and I said a prayer of hope and healing for Seth we knew we were in the midst of a loving Circle of friends and family around the world and we sensed the power in this unity. Thank you for your creativity and dedication, Kristen and Nathan.

Much love

Grandma and Grandpa (Kristen's mom and stepdad) • Winnipeg, Manitoba, Canada

Seth's Circle of

Hello Kristen and Nathan,

I'm a good friend of Ann Gray-Elton now living near Wolfville, NS. Just to let you know that my daughter-in-law, visiting from Calgary, and I will be lighting a candle with you this evening at 7 Calgary time.

My daughter-in-law's sister and her husband had twin boys two years ago in July. Reid and Andrew are vibrant cherished little guys like yours. We know of the light that little ones bring into all of our lives and wish dear Seth a long and happy, healthy life.

I will happily be making a donation to support the organization that is searching for answers for Seth and others with such a rare but challenging disease.

At the age of 63, my life is coming to an end with the diagnosis of metastasized breast cancer in my bones about 2½ years ago. At the time of diagnosis, I felt only darkness, but have been blessed since then with a journey of light and hope in concert with my family and friends. Life is such an incredible gift.

With love in our hearts,

Joan Baker and Juleta Severson-Baker

Hi Kristen,

You cannot imagine how surprised and happy I was to hear back from you, Kristen. What a gift to have you read my email out loud before the Circle of Hope began. I certainly was not expecting that, nor would I ever have thought that you would consider including it with your article in the next *Cystinosis Magazine,* but I would be honored if you did. I'm happy to know that it might support those who are touched by cystinosis.

On Thursday, I found out that I will need another round of chemotherapy and I have not yet found again the courage that I will need to go through the experience. Your email has felt like a warm hug that is helping to hold me in the light for this moment in time until I do. Thank you.

Strength for yours and Nathan's journey. With my love to you and your precious sons,

Joan

Kristen and Nathan, Leif and Seth,

My experience of Seth's circle of love in Vancouver this evening was deeply moving and powerful. The picture that you sent of you and the boys beautifully represents my feeling of the four of you as we shared these focused moments of love together with many others tonight. As well as feeling your little family so clearly and strongly, there also seemed to be a large 'glow' of energy that I've translated as the love and support surrounding Seth, and all of you, from around the globe.

Thank you for providing us all with this simple yet potent vehicle of connection.

Much love,

Carol Thatcher • Vancouver, BC, Canada

Dear Mark,

We just received your very moving email. We are sitting in a small flat in Paris and want to be part of your Circle of Hope. We have searched the entire flat for a candle, and though we couldn't find one, we did find some incense which we have lit in Seth's honor. Please know that we are thinking of you, Seth, and his parents and sending loving thoughts to you all. Please also send our best wishes to Nathan and Kristen. We are so impressed with their positive attitude and know that Seth could not be in better hands. We hope a cure will be found soon.

Much love,

Sandi and Ron Ulmi • Paris, France

Dear Nathan, Kristen, Seth and Leif,

I found myself being aware of the upcoming Circle of Hope all day, and took some time to gather just the right items to create a little shrine in honor of Seth and his family. Then at the appointed time, it was as though a switch was thrown: immediately a powerful, almost electric energy filled the room, and it seemed to faintly glow with a soft warm light. The connection with Seth – and with Leif – was so tangible. When you told me later that Seth was almost vibrating with energy during the Circle, I could well understand. Joining together with so many others around the world, holding Seth and his family in our hearts and minds, is a very real way of sharing a powerful current of hope and love. Thank you for this wonderful opportunity!

Much love, as always, to you all,

Opa/dad/Mark (Mark deBruyn; Nathan's dad)
Courtenay, BC, Canada

P.S. The little Liberty print cloth in my shrine is one of Cathy's. I deliberately included her in our Circle and know that she was with us in spirit. She loved you dearly.

Hope

Dear Kristen and Nathan,

I wasn't sure what thoughts would come to me as I sat down with my candle, although the upcoming event had been a warm and welcome idea throughout the day. At first, I enjoyed wonderful memories of Seth, Leif and you both, and of all the joyful times you have together. You are unwaveringly diligent in Seth's care, including his medication regime, and it's not always easy. But the results are there in his energy, growth and strength. As I watched my candle, I said a heartfelt thank you to you both, to the other grandparents, and members of their faithful support system, to the remarkable members of the CRF community, and to the caregivers and researchers who are working to find the cure. I really want that to happen in time for Seth, but no matter what, Seth will be an incredible human being, shaped partly by his condition, and perhaps contributing even more because of it.

With love, mom/Sherry/Gran (Nathan's mom)
Summerland, BC, Canada

Kristen and Nathan,

Such an incredible message. I don't know how you have the energy to write, never mind with such meaning.

I watched the CRF videos you sent and was so moved. They certainly give insight into what you and other families are dealing with 24/7… but are also filled with so much hope.

I have marked October 21 on my calendar. 7 pm your time is 3 am in Norway time, so I am going to wake up and think of Seth as I light a candle. You get up every night in the middle of the night, to give Seth his vitamins, so the least I can do is wake up to share in your special Circle of light.

I love you all and look forward to being with you in love and light,

Auntie Jeannette Menzies • Oslo, Norway

Hi Mark,

I have just read the email that you sent about Seth's Circle of Hope. It is 7:20 and I have just lit our candle for Seth. Thank you for including us in this Circle.

Reading about this has really touched me, first reading your letter of a year ago and now this one. I know the candle is for your grandson, but my thoughts really go to Nathan and Kristen. The way they describe their journey … the darkness, the gradual coming to terms with the 'new journey,' the 'new normal.' I can feel somewhere in the depth of my being their gut-wrenching experience and the strength that has carried them to this point … one step, one moment at a time.

It's good to hear that Seth is doing so well and we join in the hope that his good progress continues along with his angel companion Leif.

Nathan, Kristen, Leif and Seth … you are in our thoughts.

Leona (Leona Fry) • 100 Mile House, BC, Canada

Like parents around the world, parents of children with cystinosis dream that they will be able to help their children grow up to lead long, healthy and prosperous lives regardless of where their aspirations take them. Unfortunately cystinosis too frequently co-opts that vision, substituting one filled with medical and other challenges that make normal dreams far more difficult, if not otherwise impossible.

The Cystinosis Research Foundation is fortunate to work with outstanding researchers who have dedicated their lives to finding better treatments and ultimately a cure for cystinosis.

We have asked four of them to tell us about their research and a little about their personal lives. We think you will enjoy learning more about these remarkable individuals who are giving so much hope to cystinosis patients and their families.

Q&A *with Ghanashyam Acharya, PhD*

Ghanashyam Acharya, PhD
Baylor College of Medicine,
Houston, Texas

Please tell us about your background – your education, where you were born, where you currently work.

I received my PhD from the Indian Institute of Science, Bangalore, India. I was awarded a JSPS postdoctoral research fellowship to work at the Frontier Research System, RIKEN, Tokyo. I then worked as a NASA-INAC postdoctoral research scientist at Birck Nanotechnology Center, Purdue University, in Indiana. Now I work as an assistant professor in the Department of Ophthalmology and Michael E. DeBakey Department of Surgery at Baylor College of Medicine, Houston.

How did you become interested in cystinosis research?

I was introduced to cystinosis research by Dr. Jamie Jester, Dr. Stephen Pflugfelder and Dr. Jennifer Simpson.

What area of cystinosis research are you interested in and working on?

We are developing nanotherapeutics for treating corneal cystinosis.

Why is your research focus important and relevant to the overall field of cystinosis? What part of the research do you enjoy the most?

Cystinosis also causes the accumulation and rapid crystallization of cystine in the eye, leading to extreme sensitivity to light, inflammation of the eye, and eventual weakening of eyesight. We have developed a nanowafer to deliver cysteamine to

He who has health has hope.
He who has hope has everything.

ARABIAN PROVERB

the eye in a simple and most efficient way. The in vivo studies in mice revealed that the nanowafer is significantly more efficacious than the presently available eye drop treatment.

What makes cystinosis research different than your previous/ other research interests? Why is the field of cystinosis so interesting?

Cystinosis research is particularly interesting for me because there are very few other scientists working on developing new nanotherapeutics.

How would you explain the broader significance of your research? Will your research have applications to other diseases and disorders?

Our research program broadly focuses on the development of translational nanomedicine and multifunctional nano drug-delivery systems. In this area, we have developed nanotherapeutics for ocular drug delivery with specific applications in treating dry eye disease, eye injuries and infections, in addition to corneal cystinosis.

In your opinion, what is the most important question still to be answered in your area of cystinosis expertise?

The most important issue yet to be addressed is the development of more efficient strategies for the delivery of cysteamine derivatives via oral and ocular passage with negligible side effects for enhanced patient compliance.

What are your research plans for the next 2–3 years?

We are working on optimizing the nanowafer for clinical trials. We think that during the next couple of years we will see very exciting results from the trials. We are also working on developing an extended-release cysteamine nanowafer.

What impact have CRF grants had on your career? What has the funding meant to you as a researcher?

As an independent investigator, the first grant I received was from CRF. That grant gave me the support and confidence to fabricate the cysteamine nanowafer.

What progress have you made since being funded by CRF?

The cysteamine nanowafer is almost ready for human clinical trials.

We are currently preparing the necessary documentation for IND filing to obtain Food and Drug Administration approval to begin the clinical trials.

What type of scientific and medical discoveries do you see on the horizon?

Development of new drugs, in addition to cysteamine derivatives for cystinosis treatment.

How will the cystinosis community benefit from your research?

Since ours is a highly translational research program, our nanotherapeutics will provide new modalities for cystinosis treatment.

Tell us what you do in your spare time (away from the lab/office).

I spend my limited free time reading English and Indian literature, in addition to long-distance running.

Q&A with Corinne Antignac, MD, PhD

Corinne Antignac, MD, PhD
Imagine Institute
(Inserm U1163)
Paris, France

Please tell us about your background – your education, where you were born, where you currently work.

I live in Paris, where I was born. I received my MD in 1982 and PhD in 1994, both from Pierre et Marie University in Paris. I have training in pediatrics and nephrology, and worked for three years as a pediatric nephrologist in the Department of Pediatric Nephrology at Necker Hospital, where Professor Broyer was the head of the department

I then did my PhD in human genetics and set up a laboratory in Necker Hospital (Paris Descartes University) devoted to the study of rare inherited kidney diseases. The lab is now part of the new Institute of Human Genetics (Imagine Institute) on the Necker campus by Inserm and Paris Descartes University. We moved to the new building in early 2014.

How did you become interested in cystinosis research, and how many years have you been involved with cystinosis research?

Professor Broyer has long been involved in the treatment of children with cystinosis. Thus, I had the opportunity to treat several cystinosis patients when I was a clinician in the Pediatric Nephrology Department. I got involved in basic cystinosis research shortly after our group successfully identified the first gene locus of another hereditary disease, juvenile nephronophthisis (around 1995). We thought our experience in genetics could be useful in identifying the gene, and we had the opportunity to study a large cohort of cystinosis patients followed by Professor Broyer at Necker.

In collaboration with William van't Hoff and Margaret Town in London, we identified the gene involved in cystinosis in 1998. We named the protein encoded by this gene, cystinosin, and then did research to understand how it worked. We were able to show that it is a lysosomal protein and that it is able to transport cystine out of the lysosome, as Dr. Jerry Schneider and Dr. Bill Gahl had long suspected.

What area of cystinosis research are you interested in and working on? Describe what you do.

Since identifying the gene, we have tested more than 600 patients or their family members from around the world, and we have been able to show that the variability of the clinical presentation of the disease depends in large part on the type of mutations.

Then, when Stéphanie Cherqui was in the lab as a PhD student, we created the mouse model of cystinosis, which is now used around the world to study cystinosis.

More recently, we have been working on the role of cystinosin beyond the transport of cystine out of the lysosome, trying to understand why some

symptoms of cytinosis do not respond to cysteamine. We now have very exciting data showing that cystinosin by itself is involved in a metabolic pathway in the cell that can explain the development of Fanconi syndrome in children with infantile cystinosis. The research has not yet been published in a scientific journal, thus I cannot detail the work here.

Why is your research focus important and relevant to the overall field of cystinosis? What part of the research do you enjoy the most? The least?

I like doing research, but I dislike the growing burden of the administrative tasks in my daily life.

What makes cystinosis research different than your previous/ other research interests? Why is the field of cystinosis so interesting?

I very much like my research in other fields as well. Cystinosis is no different than Nephrotic Syndrome, where I am also trying to understand the disease and help the children. However, there is one critical difference: only with cystinosis do we have Nancy and Jeff Stack.

How would you explain the broader significance of your research? Will your research have applications to other diseases and disorders?

Working on one rare disease is helpful in understanding other rare diseases and even with more well-known diseases. It is clear that some of our results on the role of cystinosin could help to explain the role of other amino-acid transporters in the lysosome membrane.

Furthermore, cystinosis is the most frequent cause of Fanconi syndrome (urinary water and salt wasting). Understanding why there is a Fanconi syndrome in cystinosis will help to explain Fanconi syndrome of other origins.

In your opinion, what are the two most important questions still to be answered in your area of cystinosis expertise?

Determining why some cystinosis mouse strains develop a renal disease while others do not.

Defining the role of cystinosin in the brain.

What are your research plans for the next 2–3 years?

Better characterize the metabolic pathways we recently discovered (cf supra), which are not dependent of cystine accumulation and to find potential treatments to alleviate the burden of Fanconi syndrome in children.

Characterize the modifier genes that might be responsible for the renal disease difference in various mouse strains in the cystinosis mouse model.

What has CRF funding meant to you as a researcher?

CRF's funding has had a considerable impact on my cystinosis research (see below our main achievements).

During the past 10 years, CRF has funded a large part of our cystinosis research. (We have additional funding from Inserm and, for a short period, from the EU programs and the French patient association against lysosomal diseases.) CRF has funded the acquisition of the reagents for experiments, and allowed Zuzanna Andrzejewska to perform her PhD thesis.

It also allowed us to hire Lucie Thomas, a talented research associate, for more than five years, and to acquire a high-speed centrifuge that has been crucial to starting our search for proteins interacting with cystinosin.

What progress have you made since being funded by CRF?

We have characterized in depth the mouse model of cystinosis and showed that these mice develop a renal disease only on a specific genetic background.

We have performed genetic testing in more than 150 persons, discovered very peculiar mutations and characterized the mutations present in the late onset forms of cystinosis.

We characterized the way cystinosin is transported to the lysosome after it has been synthesized in the cell.

Mainly, as mentioned above, we have identified a set of proteins interacting with cystinosin and have shown that cystinosin has at least one additional role beyond cystine transport out of the lysosome.

Tell us what you do in your spare time (away from the lab/office).

I spend long hours in the lab, so I don't have much spare time. But when I do, I like to read, and I enjoy hiking, tennis, kayaking and sailing. And, of course, I love spending time with my sons and my grandchildren.

Q&A with Stéphanie Cherqui, PhD

Stéphanie Cherqui, PhD
University of California, San Diego

Please tell us about your background – education, where you were born, where you work now.

I was born in France in a city close to Paris. As soon as I learned about genetics at school, I became passionate about this field. I did my first internship when I was 16 at a large institute in France called Genethon, where the human genome was being sequenced for the first time. I quickly became interested in human genetic diseases and the potential of gene therapy as a treatment. Thus, I entered a very specialized and selective BS/MS program focused on human genetics at the University Denis Diderot in Paris.

I am now an assistant professor at the University of California, San Diego, where my lab focuses on the development of a stem cell gene therapy strategy for cystinosis.

How did you become interested in cystinosis research, and how many years have you been involved with cystinosis research?

When earning my master's degree, I had to do an internship in a lab. My dad, who was doing construction work in Dr. Corinne Antignac's lab, introduced me to her. After interviewing me, Corinne accepted me as an intern, where I was involved in mutation screening in a gene involved in a genetic kidney disease. I really enjoyed Corinne's lab and was interested in staying for my PhD.

Genevieve Jean had just found a deletion in a patient with cystinosis in Corinne's lab, getting them closer to the discovery of the cystinosis gene. Corinne proposed that I do my PhD on cystinosis. This was the beginning of my adventure with cystinosis. We identified the cystinosis gene in 1998, the CTNS gene, and characterized its function, lysosomal transporter of cystine. We also generated the mouse model of cystinosis, the Ctns-/- mice.

After completing my PhD in June 2002, I left for San Diego for my post-doctoral experience to learn about stem cells and gene therapy. My goal was to apply this knowledge to the development of a new treatment for cystinosis. After four years of post-doc in Dr. Daniel Salomon's lab, I became an assistant professor at the Scripps Research Institute and developed the stem cell and gene therapy project for cystinosis. I have now worked on cystinosis for 12 years.

I have been a member of the Cystinosis Research Foundation Scientific Review Board and on the foundation's Board of Trustees for more than four years.

What area of cystinosis research are you interested in and working on? Describe what you do.

My goal was to find a gene-therapy approach for cystinosis, which means correcting the disease at the gene level. Cystinosis is challenging because all tissues of the body express the CTNS gene. Thus, I decided to use stem cells that we each have in our bone marrow, the hematopoietic stem cells (HSCs), as a vehicle to bring the healthy CTNS gene to tissues. As a proof of concept, we transplanted wild-type HSCs in the Ctns-/- mice. The results were impressive. Cystine content was dramatically reduced in all organs tested, and the kidneys were preserved for the life of the mouse.

Our long-term goal is to use the patient's own HSCs and to modify them genetically to introduce a functional CTNS gene. We showed that this approach was efficient in the Ctns-/- mice and that it could lead to the decrease of tissue cystine levels and kidney

function improvement. We are now performing the preclinical safety studies required by the Food and Drug Administration to develop a phase I clinical trial for cystinosis.

We are also investigating the mechanisms by which hematopoietic stem cells that are generating blood cells could rescue a disease like cystinosis and lead to long-term tissue repair. We showed for the first time that HSCs differentiated in macrophages (phagocytic cells) within the tissues and lead to the transfer of healthy lysosomes to the adjacent deficient cells via long cellular protrusions called "tunneling nanotubes." This opens new perspectives in regenerative medicine, and we are studying the molecular components of this phenomenon.

Why is your research important to the field of cystinosis? What part of the research do you enjoy the most? The least?

Stem cell and gene therapy might become a new treatment for cystinosis. If successful in humans, it would represent a one-time treatment that would last for the life of the patient and prevent tissue damage.

Research has always been my passion. I love the excitement of discovering new mechanisms, new paradigms and new strategies that might help people who suffer from a genetic disease. For me, research is like a puzzle. Each piece I assemble brings me great satisfaction and gets me closer to a new therapy.

The part of research I like the least is the administrative duties required of the lab leader position.

What makes cystinosis research different from your other research interests? Why is the field of cystinosis so interesting?

I have worked on cystinosis for most of my research career except during my post-doctoral experience, when I focused on stem cell and gene therapy for vascular disorders. My goal was to learn about stem cells and gene therapy and apply this knowledge to cystinosis. Finding a more effective treatment for cystinosis became my mission. I know many families affected by cystinosis, and when I think about it, I see faces and smiles. It is now much more than just a research project.

Explain the significance of your research? Will it have application to other diseases?

Despite all the existing controversies, we showed that hematopoietic stem cells could treat non-hematopoietic disorders and lead to tissue repair. If our stem cell and gene therapy strategy works for cystinosis, it would represent a proof of concept for many other disorders.

The new mechanism we identified by which HSCs would lead to tissue preservation in cystinosis suggests a broader potential for HSC transplantation for other disorders for which there is no treatment.

Based on our results, we are starting a project to test this therapeutic approach for another multi-organ genetic disease.

What are the most important issues still to be evaluated in your area of cystinosis expertise?

Determining if the stem cell and gene therapy approach we optimized in the mouse model of cystinosis will also work in patients.

Many studies report discrepancies in the efficacy of treatments between mice and humans. Thus, enthusiasm should be tempered until proof that this strategy can be safely and efficiently applied to patients with cystinosis is established.

What are your research plans for the next 2–3 years?

I hope we have completed the preclinical safety studies and that we have started the clinical trial for cystinosis.

What impact has CRF grant money had on your career and on your research? What progress have you made since being funded by CRF?

The stem cell gene therapy project started because of CRF funding. This project was controversial and risky, but CRF trusted me and allowed me to launch these studies. With CRF's funding I could become an independent researcher and develop my own research projects. The first proof of concept that wild-type HSCs could treat cystinosis in the Ctns-/- mice was fully funded by CRF. The preclinical safety studies are now funded by the CRF and National Institutes of Health. The studies on the mechanisms by which HSCs could lead to tissue repair in the context of cystinosis are also funded by CRF.

What type of scientific discoveries do you see on the horizon?

I hope this work will lead to a better treatment for cystinosis. Our findings also show that HSC transplantation holds not only potential to treat hematopoietic diseases but also non-hematopoietic disorders, even complex nephropathies. This should bring new perspective in regenerative medicine and in the treatment of other genetic disorders.

How will the cystinosis community benefit from your research?

If the stem cell and gene therapy is successful in humans, cystinosis patients could benefit greatly from the treatment.

What you do in your time away from your lab/office?

My husband and I take care of our two boys, Matteo and Noah, who are 9 and 6 years old. We enjoy family time, go to the beach, to the theater, biking and traveling.

Any other thoughts about CRF or the cystinosis community?

I want to say thank you to the cystinosis community and CRF for all their kindness and support.

Q&A *with Francesco Emma, MD*

Francesco Emma, MD
Bambino Gesù
Children's Hospital
Rome, Italy

Please tell us about your background – education, where you were born, where you work now.

I was born in Brussels, where I grew up and studied. After my training in pediatrics, I moved to Boston, where I completed my fellowship in nephrology at Boston Children's Hospital. I then decided to return to Europe and for the first time moved to my own country, Italy, where I have been working since 1998. I am currently the head of the Department of Nephrology and Urology at the Bambino Gesù Children's Hospital, the largest children's hospital in Italy.

How did you become interested in cystinosis research, and how many years have you been involved with cystinosis research?

In my last year in Boston I became interested in cell transport systems in the kidney and more specifically in renal Fanconi syndrome. When I moved to Italy, I met my metabolic colleagues, who had just observed evidences in patients with cystinosis of altered glutathione metabolism, which were possibly related to the Fanconi syndrome. As I was setting up my own laboratory, we started a small project to study these aspects of cystinosis and generated our first results.

These results were supported by a grant from the Telethon Institute in Italy. Soon after, I applied for my first CRF grant.

What area of cystinosis research are you interested in and working on? Describe what you do.

In the past we have been interested in analyzing mechanisms of cell damage in cystinosis. For nearly three years we have focused on trying to find new treatments for cystinosis using an unbiased approach. Simply put, we have used easily identifiable characteristics of cells obtained from cystinosis patients and tested more than 1,000 drugs to determine those which correct the abnormal cell characteristics.

Why is your research focus important and relevant to the overall field of cystinosis? What part of the research do you enjoy the most? The least?

If successful, this research could lead to the identification of new therapies for cystinosis that could be used in conjunction with or in place of cysteamine. I cherish the design of experiments and discussing results with my team in the laboratory. Unfortunately, scientific research today also comes with considerable administrative responsibilities that add to my clinical duties. This is the part that I enjoy the least.

How is cystinosis research different than your previous/other research interests? Why is the field of cystinosis so interesting?

As a clinician, I see patients with cystinosis and have learned firsthand about their problems, their worries and their hopes. My patients are a constant reminder of the

ultimate goals of my research, and they help me to stay focused on the priorities that are relevant to them.

From a scientific perspective, despite all progress that has been made, cystinosis is still not completely understood and there is still no cure available. This is tremendously challenging and motivating for any researcher.

How would you explain the broader significance of your research? Will your research have applications to other diseases and disorders?

Many diseases share common pathways. For example, other genetic disorders are characterized by renal Fanconi syndrome. Findings in any of these disorders could apply to the entire group. More broadly, the approach we've taken over the past years for screening drug libraries may represent a model for finding treatments in other rare conditions.

In your opinion, what are the two most important questions still to be answered in your area of cystinosis expertise?

Are all symptoms related to the accumulation of cystine into lysosomes, or is the disease caused by other mechanisms that impair cell function?

Does cysteamine prevent all long-term complications of cystinosis?

What are your research plans for the next 2–3 years?

We have now identified several compounds, and one in particular seems to be beneficial in cell cultures to treat cystinosis. Our next step is to test these drugs in animal models, while continuing to search for new drugs.

What impact has CRF grant money had on your career? What has the funding meant to you as a researcher?

From the time I decided to focus on cystinosis 10 years ago, CRF has provided essential funding for my laboratory. Had it not been for CRF's support, I would not have been able to develop my research interests in this field.

What progress have you made since being funded by CRF?

Our primary achievement has been to contribute to the understanding of oxidation in cystinosis and to identify another protein that is produced by the CTNS gene, which is mutated in this disease. We are still unsure about the exact role of this protein.

What type of scientific and medical discoveries do you see on the horizon?

Obviously, we are all waiting to know if gene therapy will be a valid option for cystinosis in the near future. More generally, in recent years technological improvements have changed many aspects of how we approach medical research.

We now approach problems on a broader scale, without necessarily using hypothesis-driven strategies. While this approach considerably expands our potential to acquire new knowledge, it makes predicting new discoveries extremely difficult. Likely, much progress in understanding and treating specific diseases such as cystinosis will come from research in other fields.

How will the cystinosis community benefit from your research?

Drug discovery is a very long process. If successful, our research may identify alternative or complementary strategies for treating cystinosis.

Tell us what you do in your spare time (away from the lab/office).

I swim, bike, listen to a lot of classical music and go to a lot of art exhibitions. I am lucky because my work allows me to travel, visit many countries and meet new people.

Any other thoughts or comments about CRF or the cystinosis community?

I am astonished by all that has been accomplished, and humbled by the courage of cystinosis patients. CRF is an incredibly successful model of support for research in rare diseases, and for patients and their families. As a doctor, I will always be profoundly grateful to CRF.

The end of October marks one year since our beautiful daughter Elsie was diagnosed with cystinosis at 15 months.

Elsie's First Year with Cystinosis

By Amanda Buck, Elsie's mother
New Westminster, BC Canada

Like most people, we had never heard of the disease until our ophthalmologist informed us that there were crystals in Elsie's eyes, which confirmed she had cystinosis. I remember wondering how there could possibly be anything wrong with our perfect child. Since I first learned I was pregnant, I strived to do everything I could to protect her. Never in my wildest dreams did I think it would be Dave's and my own genes that would cause Elsie the most damage.

Suddenly we were thrust into this new world of round-the clock-medications, doctors' appointments, blood draws and a new-found fear for Elsie's future. At the beginning it was definitely a struggle coming to terms with her diagnosis. Why would something like this happen to a child? I could find no positive reason why Elsie had to go through this. The shining light during those first few months, and even more so now, is that we never felt alone.

We have been so lucky to have the most amazing and supportive people in our lives. Our family was there from the very beginning – to cry with, to vent to, and to offer support in all its forms. I don't even want to think of what it would have been like without them. Even my work was quick to offer support by donating a portion of their monthly proceeds to the Cystinosis Awareness and Research Effort (CARE) and putting up a donation box at Christmas time. With their support we raised just over $2,000!

Adjusting to Elsie's medication schedule and keeping track of all medications was another huge challenge. There were supplements that needed to be given with food, some without, and some that couldn't be given together. And then there was the Cystagon®. Since Procysbi® is not yet approved in Canada we had no choice but to go with Cystagon and it's every six-hour timeline – just when Elsie finally started sleeping through the night! For some reason the 2 am wakeup call is so much harder than the multiple, middle-of the-night cries for milk when she was a newborn.

And then there were the feeding challenges. Elsie had not grown and actually lost weight from 6 months to 1 year. Even after starting all of her medications her growth was slow, but at least she had started growing again. After being strongly urged to have an NG-tube inserted, things got worse for Elsie. I don't want to condemn the NG-tube since it has been a lifesaver for so many children and their parents, but Elsie just didn't tolerate it. She was miserable with it and put up such

a fight when we tried to feed her through it, that after a week I called the doctor and told him that we were taking it out.

We felt awful putting Elsie through it but it actually became a huge learning experience for us. There was much more work involved than we'd expected because we didn't even know what questions to ask. When it came time to discuss a G-tube we made sure we knew all the facts and were able to make an informed decision and feel good about it. We also learned to trust our instincts even if it meant disagreeing with our medical team. In the end, we are the ones who know best what our daughter can tolerate and what will work for her and us.

Shortly after that, we asked to see a nephrologist who had actually seen cystinosis patients and everything got so much better. It was a relief to have Elsie looked at as an individual with cystinosis and not treated as a typical patient. The new nephrologist also agreed that there were other avenues we could explore before having a G-tube placed. He explained that her labs and levels were all in the desired range, which wouldn't be the case if she wasn't getting adequate nutrition. Instead he recommended that we try growth hormones and reassess her later.

So far growth hormones have worked wonders for Elsie! She's grown more in the past four months than she did in the 12 months before her diagnosis. Her shoe size has gone from a size two to five and she's now in the third percentile for height and weight. Her eating continues to be a struggle but during the NG-tube week we discovered that she actually really liked taking PediaSure orally, using a giant syringe. It might look funny to outsiders but it has helped us avoid surgery thus far.

We now know that Elsie will be able to accomplish anything she puts her mind to.

There is no doubt in our minds that without the Cystinosis Research Foundation and everyone who has helped raise money and awareness, Elsie's story would have been so different. We didn't know it at the time but the first doctor to see us at BC Children's Hospital was Dr. Allison Eddy, who is on the CRF Scientific Review Board. Dr. Eddy immediately arranged an appointment with ophthalmology and we had a diagnosis. Without the tireless effort of everyone in the cystinosis community, our road to a diagnosis would have been much longer and Elsie would not be doing as well as she is today.

Elsie is a happy, energetic, typical two-year-old who just happens to take more medications and is a little smaller than most others, but that's where the differences end. A year later our fear for her future has eased significantly and we look forward to watching her grow and learn – and we now know that she will be able to accomplish anything she puts her mind to. Her future is as bright as her smile.

She Has a Future as Bright as Her Smile

i-t-a-c-f-c

One evening following our fundraiser for CRF, as I was getting Jake ready for bed he asked "I-T-A-C-F-C"?

Needing a few hints he explained that each letter is the first letter of a word. Once I revealed the first four words, "Is there a cure" I knew the rest, but he continued.

I collected my thoughts as he finished the last two words. I had just read a post by Stephen Jenkins regarding the recent studies by Dr. Stéphanie Cherqui. In second grade science language, I explained the studies in which Dr. Cherqui was able to cure cystinosis in mice. Based on the results of her experiments, we believe the same procedure will work for humans.

Jake began to imagine how the doctors would take his blood, repair the cells and then return the blood back to him. He asked questions regarding the logistics: from what part of his body would they take the blood and how many days of school he might need to miss.

He was both excited and nervous and for a few moments I took in the excitement.

Jake's twin brother Austin, Jake with his friend Logan and Professor Dumbledore.

By Amy Krahe, Jake's mom
Broadview Heights, Ohio

Jake with his twin brother Austin

This was the first time I have really talked about a cure to anyone let alone Jake. It's something you always hope for, but in your heart of hearts, can't honestly imagine in your lifetime. We have always believed with CRF driving research Jake would see incredible improvements in the treatment of cystinosis, but a cure – that may be a while.

He wanted to know if anyone had scheduled their appointment and I explained that it would take a time to develop a study for patients and when they do, it will be a process that would take more than a few days.

Since then we have had more questions and further discussions. I'm learning what many of you already know – that these questions only get more difficult to answer. The road ahead is uncertain and will be difficult at times, but one thing remains true – we are loved and supported by an amazing community.

Over 300 guests joined us on October 3 for our Harry Potter inspired Dinner & Auction raising over $95,000 for CRF. From our town to across the country, neighbors, friends, teachers and families sent us the most thoughtful letters and made the kindest of gestures and each is very special to us. Not only during our fundraising season, but all year long we are greeted with words of encouragement, prayers for healing and unwavering support. Our community continues to inspire us and give us strength. We are touched by the love and kindness we have received and will forever be grateful for the support of our community.

Hearts for Hadley

By Marcu Alexander,
Hadley's mom, Boise, Idaho

We admire the families and friends who raise money in various creative ways for cystinosis research. It's been my dream to do the same since Hadley was diagnosed with cystinosis in April 2012. My vision became a reality on September 13 when we hosted the first annual Hearts for Hadley Benefit and raised more than $60,000 for the Cystinosis Research Foundation.

Cystinosis controls many aspects of our lives. We live by a clock to administer medications every six hours, we schedule multiple blood draws and doctors' appointments each year and we can never pick up and go somewhere without thoughtful preparation and planning. There are times I resent not having more control over this disease and how it affects our family. Organizing our own fundraiser empowered me to regain some of the control I lost when cystinosis entered our lives.

We moved to Boise, Idaho a year ago to be closer to our family and raise Stella and Hadley with their cousins. Our incredibly supportive family joined forces with us to coordinate Hearts for Hadley. We wouldn't have enjoyed the same success without their love, encouragement and local connections. Our good friends, JJ and Sara Astorquia, were also a part of our planning committee. JJ took the reigns as the emcee and auctioneer for the benefit as well and did an amazing job!

The event took place at the historical Linen Building where more than 200 guests enjoyed heavy appetizers, drinks and both a silent and live auction. I was blown away by the generosity of our community and their willingness to donate to our cause. There were more than 100 silent auction items and seven live auction items including a week in Mexico, rafting trip for two on the Middle Fork and a seven course dinner for 10. The live auction was full of excitement and half of the items went twice which helped raise more money for cystinosis research!

Hadley and big sister, Stella, were on hand at the beginning of the night to greet and entertain guests. We felt it was important for new faces to meet Hadley in person while learning about cystinosis. Our event coincided with Ben's birthday so the girls surprised him with a small cake covered in hearts they helped their grandma decorate!

The evening also included a slideshow featuring many of the beautiful faces in our cystinosis community, the CRF video featuring our family and my story about Hadley's diagnosis and how far we have come in two short years. A highlight of the evening was having the Smethurst family from Logan, Utah as our special guests. Their 2-year-old daughter, Zylar, also has cystinosis. We were honored to have them with us for our first event!

Organizing Hearts for Hadley helped me regain some of the control I lost when cystinosis entered our lives.

Since our event took place in Boise, most of our family and friends from different cities and states were unable to attend. That didn't stop them from supporting our cause. We received online donations helping us nearly reach our initial goal of $20,000 before the night even began. In addition, Ben's cousin, Judy Burkhart and her husband, Tom, hosted their own Hearts for Hadley event in Seattle a week later and raised an additional $2,500 for the CRF!

I now understand how much dedication and hard work is required to organize a large fundraiser. However, the rewards are worth every sleepless night and stressful moment. It feels great knowing we are helping our community in some small way. I'm already starting to brainstorm ideas for our next Hearts for Hadley event!

Photo credit on the Hearts for Hadley Benefit go to Jimmy Blake of Blakebird Photography

Anna with her daughter Grace, 13, and son Cole, 10

A mom's struggle inspires Anna Simons to support the CRF, creating a bond to the greater cystinosis community that has only grown stronger.

I Wish All Your Wishes Would Come True

By Dennis Arp

"What is your wish?"

When Anna Simons heard that question as an attendee of the annual Cystinosis Research Foundation Day of Hope Family Conference, it made her think long and hard. Then she heard a response that came straight from heaven and she knew she had her answer.

"A girl got up and said to everyone there, 'I wish all your wishes would come true,'" recalls Anna, who attended the CRF-sponsored event to learn more about cystinosis and support friends whose lives are touched by the disease. "I thought, 'That's perfect.' I wish all the wishes could come true not just for those who have cystinosis but for the moms and the dads, the sisters and the brothers. When a cure is found, no one will have this cloud hanging over them anymore."

Anna was inspired to support the CRF with a donation of $100,000 in part because she wears her generous heart squarely on her sleeve. But first and foremost, hers is the heart of a parent.

"Basically I'm a mom who saw another mom going through a struggle," says Anna, the mother of Cole, 10, and Grace, 13.

A friend in her home community of Calgary, Alberta, introduced Anna to Karen McCullaugh and her son, Andrew, who has cystinosis.

Day of Hope
CYSTINOSIS RESEARCH FOUNDATION FAMILY CONFERENCE

Anna instantly connected with the family for a number of reasons, not the least of which is that Andrew reminds her of Cole, because the boys are about the same age and have similar personalities.

"They're these sweet, tenderhearted little souls who are compassionate to people in general," she says.

Anna also empathizes with Karen, Andrew's mom, because she knows what it's like to see your child's health and future threatened by an ailment that's difficult to diagnose. It took four years of pain and uncertainty, as well as a steady stream of hospital visits, before doctors found that a piece of Cole's umbilical cord had attached itself to his bladder, causing cysts and infection.

"I used to stay up at night and research and research, and worry and worry some more," Anna says. "It kind of takes over your life."

Now Cole is fine, but she retains "great compassion for families who struggle day by day with health issues," Anna says. "Karen is this beautiful, brilliant, brave, loving woman with two awesome kids. She and her husband have this beautiful family, and you would never know that Andrew is sick – that he has a tube in his stomach so they can inject medications every six hours.

"It all just touches my heart."

At Karen's invitation and that of CRF co-founder and trustee Nancy Stack, Anna made the trip to Newport Beach, California, and the Day of Hope conference not knowing exactly what to expect.

I left the Day of Hope Conference even more inspired to help. We need to find a cure, for these children and their families. ANNA SIMONS

As soon as she walked in, she received an extravagant welcome from families, researchers and doctors who had traveled from all over the world.

"They were all so lovely, coming up and hugging, asking me, 'Are you the Anna we've heard so much about?' she says. "It's a very special community."

The whole experience was exceptional, Anna says – from meeting new friends who are now as close as family to hearing about the progress on research that CRF support makes possible. But it all pales compared to hearing the stories and getting to interact with the children.

Anna remembers watching the young cystinosis patients play together one day when she felt a tap on the shoulder from behind. She turned and a little girl named Mary reached out to hand her a cheese cracker saying, "Excuse me, I don't want this anymore. Would you throw it away?"

It was an incredibly simple moment, but one that told Anna she had fast become a full-fledged member of the cystinosis community. It was the kind of gesture that's usually reserved for a parent or other close family member.

"I asked her if I could take her picture, and she grabbed her friends and posed, like any little girl would," Anna says.

Now Anna can't wait to return to the Day of Hope, to see her new friends from all over North America and beyond – the ones with whom she now trades calls and social-media posts – and to "hear about the progress being made with the research."

"I left there even more inspired to help," she relates, "because we need to find a cure, for these children and their families."

L-R: Alberta Allard, a close friend of Anna's; Anna Simons; Andrew Cunningham with his mom Karen McCullagh-Cunningham; his sister Kelsey; and his dad, Don Cunningham

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CYSTINOSIS
RESEARCH FOUNDATION
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A GIANT STEP TOWARDS THE CURE

Stéphanie Cherqui, PhD

The Cystinosis Research Foundation is excited and pleased to announce that we are one step closer to the cure. Dr. Stéphanie Cherqui, who has been funded by CRF for several years, recently formed the ***Cystinosis Stem Cell and Gene Therapy Consortium.***

The consortium includes experts in the fields of nephrology, neurology, endocrinology, gastroenterology, ophthalmology, bone marrow transplantation and gene therapy, and members of the cystinosis community.

Collectively, the panel will contribute to the design and methodology of a clinical trial in cystinotic patients that tests the safety of autologous transplantation with hematopoietic stem cells that have been gene modified ex-vivo with a lentiviral vector to express a functional CTNS gene.

Thank you to all CRF donors and supporters whose unwavering commitment to cystinosis research has made the consortium possible. We have more work to do but with your continued partnership, we will find the cure for cystinosis.

Consortium members include:

STÉPHANIE CHERQUI, PhD
Study Director, UCSD

- **Edward D. Ball, MD**
  Director, Bone Marrow Transplantation at UCSD
- **Nadine Benador, MD**
  Nephrology, UCSD
- **Betty Cabrera**
  Clinical Trial Coordinator, UCSD
- **Ranjan Dohil, MD**
  Gastroenterology, UCSD
- **Jeffrey L. Goldberg, MD, PhD**
  Ophthalmology, UCSD
- **Donald B. Kohn, MD**
  Hematopoietic Stem Cell Gene Therapy, UCLA
- **Robert Mak, MD**
  Nephrology/Muscle, UCSD
- **Susan Phillips, MD**
  Endocrinology, UCSD
- **Nancy Stack**
  President, Cystinosis Research Foundation
- **Doris A. Trauner, MD**
  Neurology, UCSD

Dr. Cherqui and the Amazing Lysosome-Swapping Macrophage!

By Stephen Jenkins, CRF Board Trustee and Samuel and Lars' father
Salt Lake City, Utah

Dr. Stéphanie Cherqui, of the University of California, San Diego has previously shown that if you transplant hematopoietic stem cells (HSCs) into cystinosis mice, you get stem cell engraftment with reduction in cystine in the tissues and preservation of organ function.

She is currently working on safety studies so that we can move forward with human trials with autologous HSC transplant for patients with cystinosis.

HOW DO THE STEM CELLS ACTUALLY FIX THE CYSTINOSIS CELLS?

Dr. Cherqui and her lab recently published a paper in *Stem Cells* revealing the mechanism. Several hypotheses had been suggested. Do the stem cells turn into new kidney cells, or do they fuse with the diseased cells to create a functioning hybrid? It turns out it's neither.

First you have to remember that cystinosis is a disease of the lysosome. The lysosome is like the recycling plant of the cell. It takes up old proteins, digests them into amino acid building blocks, and spits them out through transporter pumps to be reused. Cystinosin is the transporter that pumps out cystine, and if it is broken, as it is in cystinosis, then the cystine can't get out of the lysosome. Cystine builds up, damaging the lysosome and the cell. Cystinosin is probably involved in a lot of other cellular functions too, which explains why giving people cysteamine doesn't cure cystinosis. You can't just get rid of cystine; you have to replace the Cystinosin transporter somehow.

Dr. Cherqui showed that most of the HSCs turn into macrophages after transplantation. Macrophages are a type of immune cell, and their name literally means "big eater." Macrophages like to munch on bacteria, and they also clean up the big mess made by the other immune cells that are fighting viruses and bacteria. Since the macrophage is designed to clean up, it has lots of lysosomes!

Dr. Cherqui's latest research shows that these helpful macrophages respond to a distress call from the sick cystinosis cells by creating little tubes, called tunneling nanotubules (TNTs), through which they share lysosomes with the sick cells. Healthy lysosomes with the Cystinosin transporter move into the cystinosis cells, and the sick lysosomes move out of the cystinosis cells and into the macrophages. It's almost like a lysosome transplant!

This research could have big implications for other diseases. Cystinosis is just one of 50 lysosome disorders, including Tay-Sachs disease, Fabry disease, Niemann-Pick disease, Gaucher disease and metachromatic leukodystrophy.

What if HSC transplantation could swap out the broken lysosomes in these diseases? It's interesting to note that lysosomes aren't the only organelles that move across the tunneling nanotubules. Dr. Cherqui and other researchers have also noted mitochondria making the trek. Mitochondria are the "powerhouse" of the cell, where most of the energy required for cellular function is generated. There are many mitochondrial disorders, and it is possible that HSC transplantation could be used to treat these as well.

The cure for cystinosis could be the cure for a whole host of genetic diseases!

I still remember the day in 2011 when Ashton came home from the Cystinosis Research Foundation Day of Hope conference and told me that a scientist had cured cystinosis in a mouse model with hematopoietic stem cell transplant. Hematopoietic stem cells, or HSCs, are the stem cells in the bone marrow that develop into blood cells, including the red cells that carry oxygen, and the white cells that make up our immune system.

How to Cure Cystinosis

I had just finished my hematology block in medical school, and what Ashton was telling me sounded preposterous. Bone marrow transplants are definitely effective for certain blood diseases like leukemia, multiple myeloma and immunodeficiencies, but it didn't make any sense that stem cells destined to become blood cells could repair damaged kidney, liver, muscle and thyroid tissue. *Boy, was I wrong!*

In 2009 Dr. Stéphanie Cherqui showed that if you give a cystinosis mouse a bone marrow transplant, it leads to reduction of cystine in all organs, including the cornea, and preservation of kidney function. She showed the same thing in cystinosis mice that received a HSC transplant. The effect was still present 15 months after the transplant. This paved the way for FDA approval for a bone marrow transplant trial for cystinosis, which is still waiting to enroll its first patients.

The idea of curing a genetic disease like cystinosis with an allogeneic bone marrow or HSC transplant is pretty exciting. But bone marrow transplants are not risk-free. The biggest complication is graft-versus-host disease, where the transplanted bone marrow cells actually attack the recipient, leading to severe skin, liver and gastrointestinal disease. You also have to kill the patient's bone marrow before transplant with chemotherapy, putting the patient at high risk for infection.

Thankfully Dr. Cherqui has found a way around this.

Rather than giving the patient someone else's hematopoietic stem cells, she proposed taking the patient's own blood, genetically modifying the stem cells to express the correct Cystinosin genes, and reintroducing the blood as an autologous transplant. This creates a perfect match, eliminating the risk of graft-vs-host disease, and reducing the intensity of chemo to suppress the bone marrow prior to transplant.

In 2013, Dr. Cherqui published research showing she had found a way to deliver the correct Cystinosin gene to stem cells with a virus. The virus goes into the cell and copies its DNA, including the correct Cystinosin gene, into the stem cell's DNA. The stem cells were then transplanted back into the mice from which they were taken, and these cystinosis mice had the same reduction and cystine and organ preservation as the mice that got allogeneic HSC transplantation.

With these amazing results, Dr. Cherqui has now moved toward clinical trials in humans, and is currently working on safety studies for the FDA. Hopefully in the next few years there will be a trial for autologous HSC transplant in actual patients.

All of this is possible because of the Cystinosis Research Foundation, which has funded Dr. Cherqui's research. We are grateful for her tireless dedication. I won't be surprised when she receives the Nobel Prize.

The cure for cystinosis is coming!

Night at the Park WITH SAM & LARS

We got back from the 2014 CRF Day of Hope in April bursting with excitement and enthusiasm. We spent the whole drive back to Utah brainstorming on what we could do for a fundraiser. We were so grateful for everything that the Cystinosis Research Foundation has done for us, and for all the incredible research that it is funding, so we really wanted to do something to give back, even if it was small.

The biggest issue for us was the time crunch. I was going to graduate from medical school in a month, and starting residency training a month later. We had a small window five weeks out that we decided was our best bet.

But what kind of fundraiser can you do with basically no budget? We didn't feel like we had the time or resources to do a big gala. Eventually we decided to reserve the pavilion at our boys' favorite park, Lindsey Gardens. We planned to sell Italian sodas or something simple like that, with a silent auction.

We started visiting businesses with a letter requesting auction items. We had modest success using this method, but it took a lot of time, so finally we switched to shotgun e-mailing local businesses. After sending more than one hundred e-mails and letters, items started pouring in. When family and friends heard about our event, they also started offering auction items.

A week before the event we had over 100 items, ranging from tickets to the zoo and a Salt Lake Bees baseball game to outrageous socks, beautiful paintings and quilts.

Our good friends Tom and Megan Dunford have a soda cart business, Dunford Sweet Cream Soda. When they heard about our event they asked if they could make cream sodas for free.

A local bakery, Ruby Snap surprised us with a donation of more $400 in gourmet cookies to sell at the event.

Finally the big night arrived. Set up was a bigger task than we anticipated. Luckily we had two friends, Rachael and Allyson, who drove from Arizona for the event, and they came to our rescue. They helped Ashton get all the decorations and auction items arranged while I drove back and forth to our house to get auction items. Our families showed up to help, as well, and pretty soon everything was out.

At the start we had some trouble with wind, which sent auction items and bid sheets flying, but everyone persevered and had a great time.

Family and friends from all over came, and they brought their friends too. People I had never met were initiating bidding wars and racking up dollars for us. The cream sodas were a hit, especially the raspberry flavor.

Anina, a wonderful girl from our neighborhood, sold cookies that went quickly. My sister, Sarah, made hundreds of cake bites that sold out fast, and Ashton's sister, Whitney, brought wildly popular Rice Krispies Treats. Our friend Cynthia sold tons of delicious sugar cookies.

When the auction tables started timing out, hordes of people mobbed us at the donation table, and luckily my calm, collected dad was there to keep track of all the money that was pouring in.

We were blown away by everyone's generosity. One family, the Alexanders, bought all the items that no one else had bid on. Before you knew it people were packing up with their prizes and clearing out.

We couldn't wait to get the kids in bed that night so we could count the donations. That night we totaled more than $13,000 in donations,

and over the next couple weeks, we received even more, for a grand total of $17,000.

Thanks to the kindness and generosity of our many friends and family members, we far exceeded our goal. Thanks to CRF, every dollar will go directly to scientists like Dr. Stéphanie Cherqui to find a cure for cystinosis.

Thank You

YOUR WONDERFUL OUTPOURING OF LOVE HAS GIVEN US THE STRENGTH TO KEEP LIVING WITH CYSTINOSIS EVERY DAY. WE HAVE SO MUCH HOPE FOR OUR BOYS AND THEIR FUTURE.

ASHTON AND STEPHEN JENKINS,
SAMUEL AND LARS' MOTHER AND FATHER
SALT LAKE CITY, UTAH

A GRANDPA'S *Wish*

Tina with her Papa Richard Fuchs

The large calloused hands of the 6'2" man, towered over the tiny frame of such a little girl. Although his size was intimidating, she knew to have no fear of this "gentle giant."

The familiar words: "Where's papa's hug?" always preceded uncontrollable giggles. Her favorite was playing hard to get. They were a perfect match for each other – one just as ornery as the other. So much alike, both faced with countless challenges, but both so selfless and loving. There is no better way to describe precious little Tina and her grandfather, Richard.

I recall the days when Mark and I were nervous, wondering if Tina would be able to make it through the night. "Papa" Richard would travel seven hours just to see his little sweetie as she lay suffering in the hospital. Whenever she saw him, she would use all of her strength to pull herself up the tall bars of the crib, and would manage a smile through the many tubes coming out of her nose and mouth. Tears would begin filling his eyes as their eyes met. That was his "partner in crime," and his heart was absolutely crushed when he learned of her diagnosis. Over the years many hospitalizations followed and he and grandma Dona were always there to cheer Tina up.

Papa Richard always had a jovial spirit, but when he was with Tina, it was more prominent than ever. The constant teasing always brought a smile to my face and I would have to remind him that he was the adult in the relationship.

Papa Richard I love you

By Denice Flerchinger, Tina's mom, Clarkston, Washington

Papa Richard had his own health issues, but when kneeling down to pray at night, his first prayer would always be that God would take away all of Tina's suffering. His heart was enormous, and his love for her was unbelievable. He wanted her to be cured and always believed she would be.

On June 9, 2014, the world lost a beautiful soul, and Tina lost her beloved Papa. Papa Richard has left such an imprint on this little girl's heart. Whenever I find myself crying, Tina is always quick to remind me not to be sad because "grandpa is in Heaven, now we will have a cure!"

Everyone who knew my father knew about his precious granddaughter, Tina. Papa was always Tina's biggest cheerleader and he always will be. We know he's in Heaven pleading with God for a cure. My dad and mom have been a huge part of our success in the continued support for cystinosis research through Tina's Hope for a Cure.

Papa's in Heaven pleading with God for a cure.

The very last time Tina had the opportunity to see her Papa Richard, he was the one in the hospital. Her heart was broken, but his face lit up when she gave him the bracelet she had so lovingly spent hours making for him. As he looked in her eyes he vowed to never take it off – and he never did.

Papa Richard's spirit continues to live in Tina.

Papa Richard, Tina and Grandma Dona

Tina is now in fifth grade and continues to take on her own challenges every day, just like her Papa – with a big smile and an ornery spirit. We still await a cure, but we have so much hope. Papa Richard's friends donated $4,000 to cystinosis research in his honor.

Until we meet again Papa Richard we all love you to the moon and back.

to the moon and back.

By Katie Monaghan,
Abbi's mother,
St. Catharines,
Ontario, Canada

Eat for Abbi

A Cystinosis Pasta Night Fundraiser

This year Abbi turned 8. Wow! We have come a long way since that scary day in October 2007 when she was diagnosed. I still feel the pain. It stings in the back of my throat.

Cystinosis often brings new challenges but Abbi isn't fazed by them. She rides her bike to her friend's house; she swims in the deep end of the neighbor's pool and now reads novels after struggling with reading last year. Medications are added as the cystinosis progresses. It takes time for Abbi's body to adjust causing many days absent from school, but Abbi still produces a stellar report card. She has also begun a course of growth hormones to help her catch up with peers.

There are no breaks from cystinosis with round-the-clock medication schedules, surgeries from side effects, and ongoing concerns as Abbi grows older and new problems arise. It's a busy life keeping up with appointments, medication schedules, work, school, meals and activities – all while maintaining a social life and ensuring that everyone gets enough attention.

Now enters Abbi's 17-year-old cousin Meghan, who asked if she could have a fundraiser for cystinosis. I said "No," explaining that we didn't have time – but Meghan is a persistent young lady who wouldn't take no for an answer. She promised that she and her friends, Justine and Ruth-Anne, would take it on.

That's how *Eat for Abbi* was born!

Abbi with her 17-year-old cousin Meghan

Abbi is special to Meghan, and Meghan is special to Abbi. Abbi is exceptional to all of her friends and family. *Eat for Abbi* was going to bring them all together for a good cause and a little fun. The plan was simple: share a meal, dole out prizes, keep it inexpensive for guests and raise money for cystinosis.

Meghan is a natural leader. She's organized, works hard and believes in planning her work and working her plan. With Justine and Ruth-Anne, and help from other friends and family members, the event was sure to be a success.

There were meetings to monitor progress, with Meghan and her trusty folders filled with lists assuring that everything was checked and rechecked: When will the event take place? Where will it be held? Who will plan it? Who will do the work? Who will donate prizes? Meghan managed it all while balancing school, family responsibilities, three part-time jobs and her social life.

Once the date was chosen, tickets were widely distributed and they sold like hotcakes.

Finally the big day arrived! On May 13, balloons welcomed guests into the decorated hall, with abundantly laden prize tables and the delicious aroma of Italian food. The buffet-style brigade line – run by student volunteers – flowed smoothly throughout the night allowing guests to quickly receive their salad and tasty entree.

Sophie and Abbi at their bracelet stand.

Abbi's mom and dad, Terry and Katie Monaghan, with Meghan, and CRF Board Member Jody Strauss and her husband Trevor from Waterloo, Ontario, Canada.

Prize tickets were easy to obtain and sales boomed. Beaming, Abbi and Sophie made and sold bracelets from their own stand at the entrance.

When the night drew to a close, thanks were extended to everyone who helped. An exhausted Abbi was whisked away to home and her bed, while the cleanup crew stayed until the last crumb was swept up.

Through the community's remarkable generosity more than $15,000 was raised – an astonishing amount for a mighty young woman not yet out of her teens.

Meghan and her friends have been recognized for their amazing efforts by friends, family, school officials, media, as well as the cystinosis community near and far.

And the Monaghan family continues to be overwhelmed by the love and support we receive from Meghan and her peer's for Abbi and the cystinosis community.

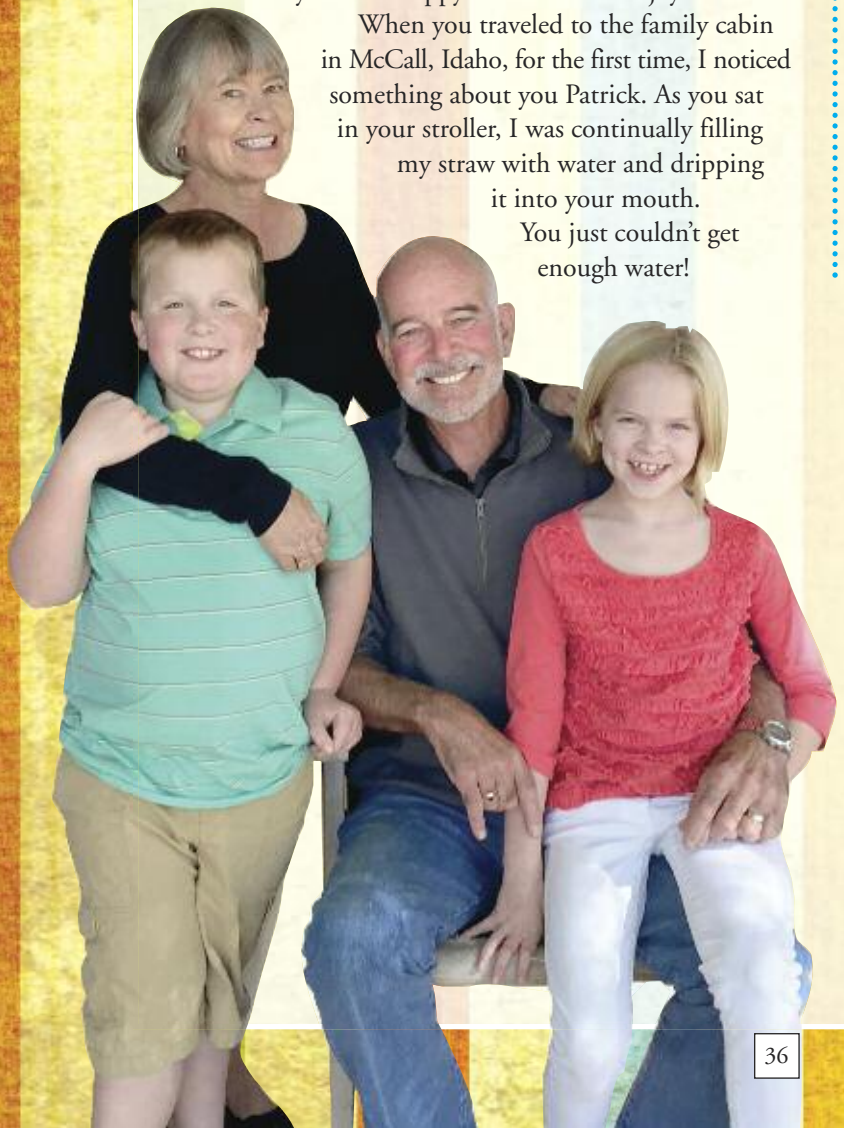
***It takes a village,* and ours is growing!**

Especially for Jenna and Patrick

How fantastic that you will soon celebrate your 10th birthday. Grandpa Doug and I remember how excited we were when we heard that your mom and dad were having twins! Patrick, you were the first born, and a minute later, Jenna – two beautiful chubby babies.

You slept nose to nose during those first days, already bonded in your life together. But something was peculiar. Your dad asked, "Why are the sheets always so wet?" And your mom wondered if all parents bought as many diapers as she did. Still, you were happy little ones and a joy to all.

When you traveled to the family cabin in McCall, Idaho, for the first time, I noticed something about you Patrick. As you sat in your stroller, I was continually filling my straw with water and dripping it into your mouth. You just couldn't get enough water!



Jenna, at 13 months you were in the hospital with a virus. The doctors treated you as they had been trained to do but you got sicker. After many tests we learned that you had a kidney problem and a serious condition called cystinosis. Patrick, you were then tested and, sure enough, you also had cystinosis.

We were shocked to hear that you had a rare disease that none of us had ever heard of. It is called an "orphan" disease because so few people in the world have it – even most doctors don't know about it.

But something wonderful happened. Your dear friends (especially Ron Thomas, Andrew Sackhiem and Uncle Tommy Walcott) started a foundation to find a cure. Jenna and Patrick's Foundation of Hope is supported by many family members and friends who care about you and others with cystinosis. Now you both attend the foundation's *Swing and Bling* events in Sacramento, where to date $1.4 million has been donated to fund research. Jenna, I know that you like dressing up for this special occasion; and Patrick, I know you just hate dress shoes and a tie! I am humbled and in awe of these events and all the caring people who donate.

The money your foundation raises is presented to the Cystinosis Research Foundation at its Natalie's Wish Gala each year. Millions have been donated to CRF, which has now funded more than 122 research studies. The Stack family is responsible for starting CRF, which has become a community of doctors, researchers, patients, families and friends all working together to find a cure for cystinosis.

Story by Jan Batt
Jenna and Patrick's maternal grandmother
Caldwell, Idaho

You are fortunate to be part of a group of people who give so much of themselves to help you. And you are also blessed with loving parents who are both remarkable individuals.

From the beginning your mom and dad learned everything they could about cystinosis. Now they are on the board of CRF and they work every day to help you deal with your disease and to find the cure. But they will not let cystinosis define you. They expose you to many life experiences and do not allow you to use cystinosis as an excuse. I think this contributes to your positive outlook and your desire to live life to the fullest.

Of course, you can't utter the word cystinosis without mentioning the meds. They are not an option but a fact of life. I admire both of you for taking the bad-tasting medicines without complaining. Continue to take your medicine, chase it with water and treat yourself afterwards. And promise me that you will always take the medicine to keep cystinosis under control. Already, research allows you to take meds every 12 hours instead of every 6 hours. And you are now old enough to take the yucky pink medicine in pill form.

It's not easy for you to live with cystinosis but I am thankful that you can share it with each other. As fourth graders, I know you wished that you could go to friends' homes without concern. I know how you hate being wet at night.

Your teachers and parents know what you are dealing with so they have arranged for tutors to help you stay at grade level. It isn't because you aren't smart – it's because sometimes you don't feel well at school, you get tired easily and you continually have to make trips to the restroom!

Forget cystinosis for a minute. Let me tell you what I see in you as children. Jenna, you are a kick!, the "energizer bunny" – a girly girl who likes nothing more than to wear pretty dresses and give your friends a makeup session. You are a tough one though, keeping your feelings to yourself, except for shedding a tear when your summertime in McCall comes to an end. Your love of animals is so enduring. At SPCA camp, you wanted to help all the critters – and even take them home with you.

Patrick, you have such a passion for roller coasters. I am amazed that you know the names and locations of the world's best roller coasters, and by your desire to ride them all. I want to be in Ohio when you ride the fantastic one there. And, you have such a loving spirit. At any given moment you will say, "I love you so much Grandma." Who could ask for more from a grandson?

It's okay that school sports are a bit more than you can handle at this time. Keep doing what you can. I'm proud that both of you are such good swimmers and that you tackled the climbing wall this summer. Keep active on your bikes, scooters and roller skates. I love that you keep track of your steps with your wrist pedometer, Patrick.

I know that your strong faith will guide you along life's path. Cystinosis may make life harder at times, but remember God is always with you and that He has a special plan for each of you.

Patrick and Jenna, your Grandma Jan and Grandpa Doug are so very proud of you. You are very special people.

We love you!

A Journey to Hope

About ten years ago, Patrick and Jenna entered our lives. They were grandchildren numbers eight and nine, and they were very much wanted and adored. Twins! Now this was a grand new experience and we savored the adventure. We have not been disappointed.

At 15 months our journey took a detour when we learned that genetics had gone awry and the twins had cystinosis, a disease we had never heard of. The online information we read was not encouraging. Jenna and Patrick were terribly sick and worst of all, there was no cure. It was devastating.

"In God we live and move and have our being. He knows our joy and rejoices in our rejoicing. He knows when we suffer and shares our suffering. He created us and we are not a matter of indifference to him."

MONSIGNOR ROMANO GUARDINI

God has put his work into people's hands, for them to maintain and continue. I believe God wants each of us to complete this work for His joy and to give meaning to our lives. So, God sent us Nancy and Jeff Stack, with all their wisdom and experience, to work with Jenna and Patrick's parents, Kevin and Teresa. True "saints" in our midst, Nancy and Jeff offered a wealth of information on managing the daily routine that comes with raising a child with cystinosis. They knew the medicine routines, about the mountains of laundry, and where to head for more help. They were also dedicated to fulfilling the wish made by their daughter, Natalie – to make the disease go away forever. Nancy and Jeff decided to form the Cystinosis Research Foundation, which would change this orphan disease, one that previously benefited from little or no research, into an active organization, funding research that would lead to a cure. CRF has given real hope to all of us. What an amazing ten years this has been!

St. Augustine said, "You are impatient; but what seems a long time coming to you will soon come to pass. It is infirmity that makes our wait seem long when it is really short. Nothing seems so long as the mixing of medicines for someone who needs them."

Story by Juanita Partington,
Jenna and Patrick's paternal grandmother
Upland, California

Patrick and Jenna's 4th grade school pictures, September 2014.

Soon, we met our knowledgeable and dedicated doctors. Dr. Jerry Schneider and Dr. Ranjan Dohil quickly became household names. They worked long and hard to help the children with cystinosis and to formulate new treatment methods.

Next, we met Dr. Stéphanie Cherqui at the CRF Day of Hope Family Conference, where she reported that her mouse study research showed great promise. Soon, we heard about Dr. Jennifer Simpson's nano-wafer for eye care and of Dr. Ghanashyam Acharya's patch delivery approach for cysteamine. The breaking of the genetic code has opened new doors for treatment – all of it like something out of a science fiction magazine!

The most immediate change came when Jenna and Patrick started taking Procysbi® and at long last, the family experienced a full-night's sleep, something that had not happened in nine years.

During these last nine years our circle of friends has expanded! Other cystinosis families, once strangers, are now old friends with special stories to tell. Each family's path to diagnosis is strangely similar, but seeing the other children's progress is encouraging.

Most of all, I am greatly humbled by the caring, the generosity, and the hard work of the many families and friends who raise research funds to keep the quest for a cure moving forward. These special people have blessed our lives and we are privileged to know them.

This year at Easter break Grandpa and I spent time in Newport Beach with Kevin, Teresa and Jenna and Patrick. At nine, Jenna and Patrick's lives have become a unique kind of normal. Yes, they still take massive amounts of medicine and there are days when they do not feel good. But there are also days like those we spent digging in the sand, traveling to the Long Beach Aquarium, riding Segways and going to Disneyland.

Like other kids, they had homework assignments and math projects to complete. Thanks to their wonderful parents, Jenna and Patrick are normal kids who have learned to cope with a serious illness, and to get on living life.

Often, what seems to be bad also brings blessings. Jenna and Patrick's illness has taught us what is most important in our lives – faith, family and friends, and the time to enjoy them. We live in the present and deal with problems one step at a time. We savor the moment!

For now, I give thanks for the progress that has been made and I look forward to the cure that is yet to come. Until that moment, may God hold us all in the palm of His hands.

Day of Hope

CYSTINOSIS RESEARCH FOUNDATION
FAMILY CONFERENCE

Thursday, April 16 – Saturday, April 18, 2015
Balboa Bay Resort,
Newport Beach, California

Our 2015 *Day of Hope Family Conference* will take place over three days and culminate on Saturday night at the Thirteenth Annual Natalie's Wish Celebration.

The Day of Hope Family Conference will feature progress reports from CRF-funded researchers and sessions from clinicians. Speakers include (confirmed at time of publication):

Dr. Ghanshyam Acharya and Dr. Jennifer Simpson: Corneal cystinosis and novel nanowafer technology

Dr. Bruce Barshop: Cystine testing and measurements

Dr. Stéphanie Cherqui: Autologous stem cell transplantation and gene therapy

Dr. Francesco Emma: Novel treatments for cystinosis

Dr. Paul Grimm: Chronic kidney disease and treatment; teens and cystinosis

Discussion Panels:
Parent Panel • Teen and Adult Panel • Medical and Researcher Panel

All families are encouraged to participate in discussions and question and answer sessions. Families will have a chance to meet, socialize and share their personal stories of life with cystinosis.

CONFERENCE SCHEDULE

Thursday, April 16
Check-in at the Balboa Bay Resort
Welcome reception and family dinner

Friday, April 17
Conference sessions
Followed by a family dinner celebration

Saturday, April 18
Conference sessions
Family lunch and social time

Saturday evening plan to join us at our **Spectacular Natalie's Wish Celebration.**

More information to follow in 2015, or contact Nancy Stack at nstack@cystinosisresearch.org

CYSTINOSIS RESEARCH FOUNDATION | RESEARCH HOPE CURE

if life gives you lemons...

By Jody Strauss, Gabbie's mom
Waterloo, Ontario, Canada

Delaney, Elly, Gabbie and Chloe

Some of Gabbie's biggest supporters come in the smallest packages. Working together, eight-year-old Elly Ruchty and seven-year old Delaney Laking, were busy this past summer planning not one, but two neighborhood lemonade stands and cupcake sales!

The two events combined raised $221. Delaney said that she and Elly initiated the fundraisers, "To help make money for a cure for cystinosis and help make kids happy and feel better."

Elly added her hopes for Gabbie, "I hope when the doctors find a cure you will feel much better."

The love and support from these two very special girls has touched our hearts. We were amazed that even at a young age, Elly and Delaney have made a difference in our community by providing important research money for cystinosis. Thank you Elly and Delaney!


Amanda Kuepfer, Gabbie Strauss, Elizabeth Anne Kuepfer, Chloe Strauss

Mahlon and Rachel Kuepfer saw the annual Millbank Community Garage Sale as an opportunity to raise money for cystinosis. On Saturday May 31, 2014 the Kuepfer Family sold charcoal barbecue sausage and hot dogs on buns, cold pop and water and their famous homemade donuts. They also sold garage sale items. Their hard work paid off. The combined effort from the barbecue and garage sale raised $2,253.32!

We are so grateful for this family and the Millbank community for raising money to find a cure for cystinosis.

A wise man once told me the secret was to

surround yourself with good people and good things will happen.

By Erin Little, Olivia's mom
Port Elgin, Ontario, Canada

On September 20, the day of our Second Annual Swing, Shoot and Liv Golf Classic, that statement held true when Saugeen Golf Club in Port Elgin, Ontario was filled with 216 eager golfers despite the pouring rain.

Golfers embraced the rain – there was not a single complaint or unhappy person that day as the thunder rolled and rain poured down, a true testament to our community. Complete strangers stood in line waiting to be served lunch. They offered each other a dry place under their umbrella and happily held open a door welcoming them to a dry place, all for a little girl named Olivia.

Our family took a big chance this year, opening our doors to our community so it could learn who we are and to hear our story. From the beginning, we have been afraid about raising awareness and funds for cystinosis. Our biggest fear: no support from our community because we weren't sure our little town would stand behind a cause so rare that it affects a very small population. Boy, were we wrong!

Community is defined as a group of people living in the same place or having a particular characteristic in common. Our small community of approximately 12,000 people proved to us what a community can accomplish if we all work together. I say this over and over to everyone we meet and share our story, Chad and I can provide Olivia with the best care she deserves and we can spread awareness, but we need everyone to come together and stand behind us to find a cure.

We couldn't do it without you …

The Butcher, who held our first charity barbecue – raising more than $1,000 while encouraging others to help our family fight cystinosis.

The Grocer, who challenged the entire community to give to help fight cystinosis, raised $6,000 and the word cystinosis spread like wild fire.

The Energy Maker, who put himself out there and became an honorary chairman for the *Swing, Shoot and Liv Golf Classic,* which raised $100,000.

Continued on next page

The Waitress, the kind and loving woman who worked tirelessly all day and then handed over her earnings to beat cystinosis. $75 may seem so small but we can't get to a million without the first $75.

The Bride and Groom, who crashed our golf classic to hand over a donation in lieu of gifts for $600.

The Hockey President, who gave up a round of golf with the hockey team to raise funds for cystinosis – two tournaments in the record book raising over $120,000.

The Grandpa, who won the wagon of wine only to donate it back again to the Live Auction.

The Neighbors, who love our children and sacrifice their time to play with them. Who go to work every day and spread awareness and speak so highly of our cause.

My Uncle, who puts all of his jobs aside to do one last project for the tournament.

My Sister and Brother-in-law, who drove hours to be with us and take amazing photos.

My Girlfriend, who sacrificed her days getting personal things done to tie ribbons, make decorations, cut hearts and a million other things.

Our Family and Friends, who stand behind us every step of the way.

The Volunteers, who selflessly give their time, energy and love.

Saugeen Golf Course, for being so caring, patient, kind and understanding and the biggest thank you for letting us golf when the weather wasn't on our side.

The Strangers, who we now call family and who are officially part of Team Cure Cystinosis.

My Husband Chad, for being the pillar of strength in our house.

Harper, for being the best little sister.

Olivia, for being her sweet, strong and innocent self.

We put our fear aside and asked for support – and what we got was love, kindness and generosity. **Thank you to everyone who supports cystinosis.**

It's not about what it is, it's about what it can become.
Dr. Seuss

A version of this article originally appeared on Kincardine News on October 1, 2014
http://www.kincardinenews.com/2014/10/01/areva-charity-baseball-tourney-raises-over-5500-for-liv-a-little-campaign

AREVA BASEBALL TOURNAMENT RAISES $5,500 FOR CYSTINOSIS RESEARCH

By Lisa Umholtz

AREVA hosted a charity baseball tournament to raise awareness and funds for the Liv-A-Little Foundation, an organization that raises money for the Cystinosis Research Foundation, at Connaught Park on September 25, 2014.

The event raised $5,543 for the Cystinosis Research Foundation (CRF).

Only 2,000 people in the world have been diagnosed with this very rare disease. Five-year old Olivia Little of Port Elgin was diagnosed with cystinosis at age two.

AREVA Vice President Larry Robinson, said he wanted to raise awareness and funds for the CRF after recently meeting the Little family and Olivia.

He challenged Harry Hall, Vice President Supply Chain at Bruce Power, to a baseball game, and before he knew it, he had a full-fledged competition between AREVA, Bruce Power and Superheat employees.

"Every dollar raised goes directly to research, which you don't typically see," Robinson said of the CRF.

Larry Robinson, VP AREVA (left), introduced five-year-old Olivia Little, who was diagnosed with cystinosis at age two, and her mother Erin, father Chad, and sister Harper. Olivia threw the game's first pitch.

The event was organized by AREVA staff and put on by volunteers, including a licensed bar beside the baseball diamond run by the Kincardine Cubs and a bake sale by members of Community Living Kincardine and District.

AREVA and Bruce Power staff raised $520 and $570 respectively prior to the tournament, with all funds going to the CRF.

Olivia Little was on hand to open the event by throwing the first pitch with her mother Erin, father Chad, and sister Harper.

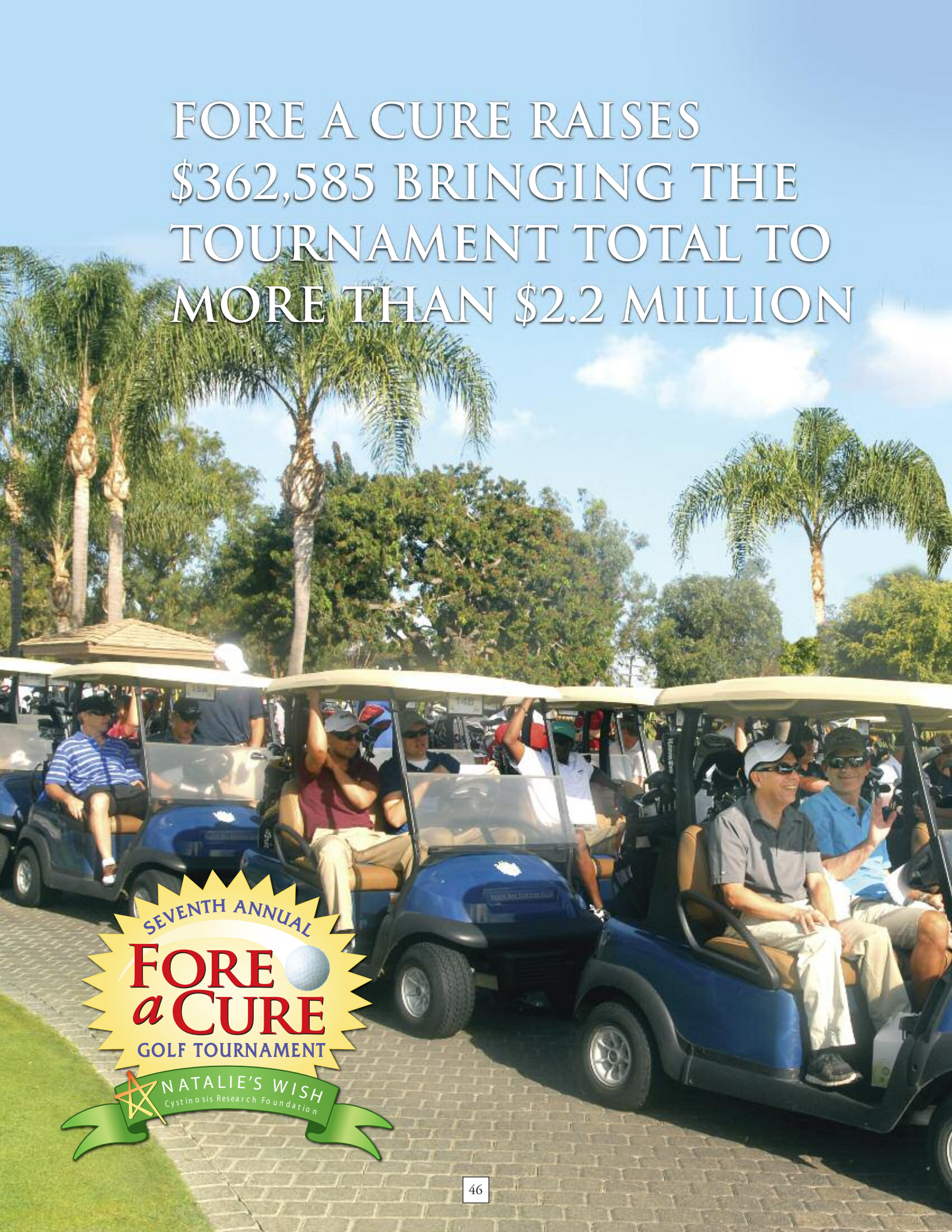
The Liv-A-Little Foundation and the Cystinosis Research Foundation would like to thank AREVA for its exceptional generosity. With the help of AREVA and a growing number of other supporters we are moving ever closer to a cure for cystinosis.

Visit www.livalittlefoundation.com for more information about cystinosis, Olivia Little or her foundation.

LIV-A-LITTLE FOUNDATION

AREVA is a leader in Canada's uranium production and leading manufacturer of radiation measuring equipment, and as a services and engineering provider for nuclear reactors. AREVA's office in Kincardine, Ontario was the sponsor of the baseball tournament featured in this story.

FORE A CURE RAISES $362,585 BRINGING THE TOURNAMENT TOTAL TO MORE THAN $2.2 MILLION



The Natalie's Wish Fore a Cure Golf Tournament, celebrating its seventh year, had another record-breaking event at the exclusive Santa Ana Country Club. Led by its dynamic Chairman Vince Ciavarella, a powerhouse golf committee, an amazingly dedicated group of volunteers and the generous sponsorship support of more than 200 companies and business leaders, the tournament raised $362,585 for cystinosis research.

"The exceptional support and generosity of our friends and community has enabled CRF to make significant advances in the treatment of cystinosis. CRF-funded researchers at institutions around the globe are making important breakthroughs toward the cure. We are honored to be a part of the progress to help Natalie's wish become a reality by contributing to cystinosis research," said Vince.

The event brought many past sponsors and golfers, as well as many new supporters and we are grateful to everyone who participated. The tournament's reputation as "the best in Orange County" was confirmed as sponsorships were sold out several months in advance, and because of our dynamic golf committee all of the underwriting opportunities were completely sold by tournament day.

Since 2007, the Fore a Cure golf tournaments have contributed more than $2,233,585 to cystinosis research and the quest for a cure.

Our dedicated committee and volunteers, most of who have been involved since the beginning, are the driving force behind the tournament. Their efforts helped make the 2014 event the most successful ever.

SEVENTH ANNUAL FORE a CURE GOLF TOURNAMENT
NATALIE'S WISH Cystinosis Research Foundation

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THE RESORT AT
PELICAN HILL
NEWPORT BEACH

Mark your calendar for next year's Fore a Cure Golf Tournament, which will be held at the world-class Pelican Hill Golf Club on Monday, October 19, 2015.

For sponsorship information contact Zoe Solsby at (949) 223-7610 or zsolsby@cystinosisresearch.org.

Henry is Busier and Bigger by the Day

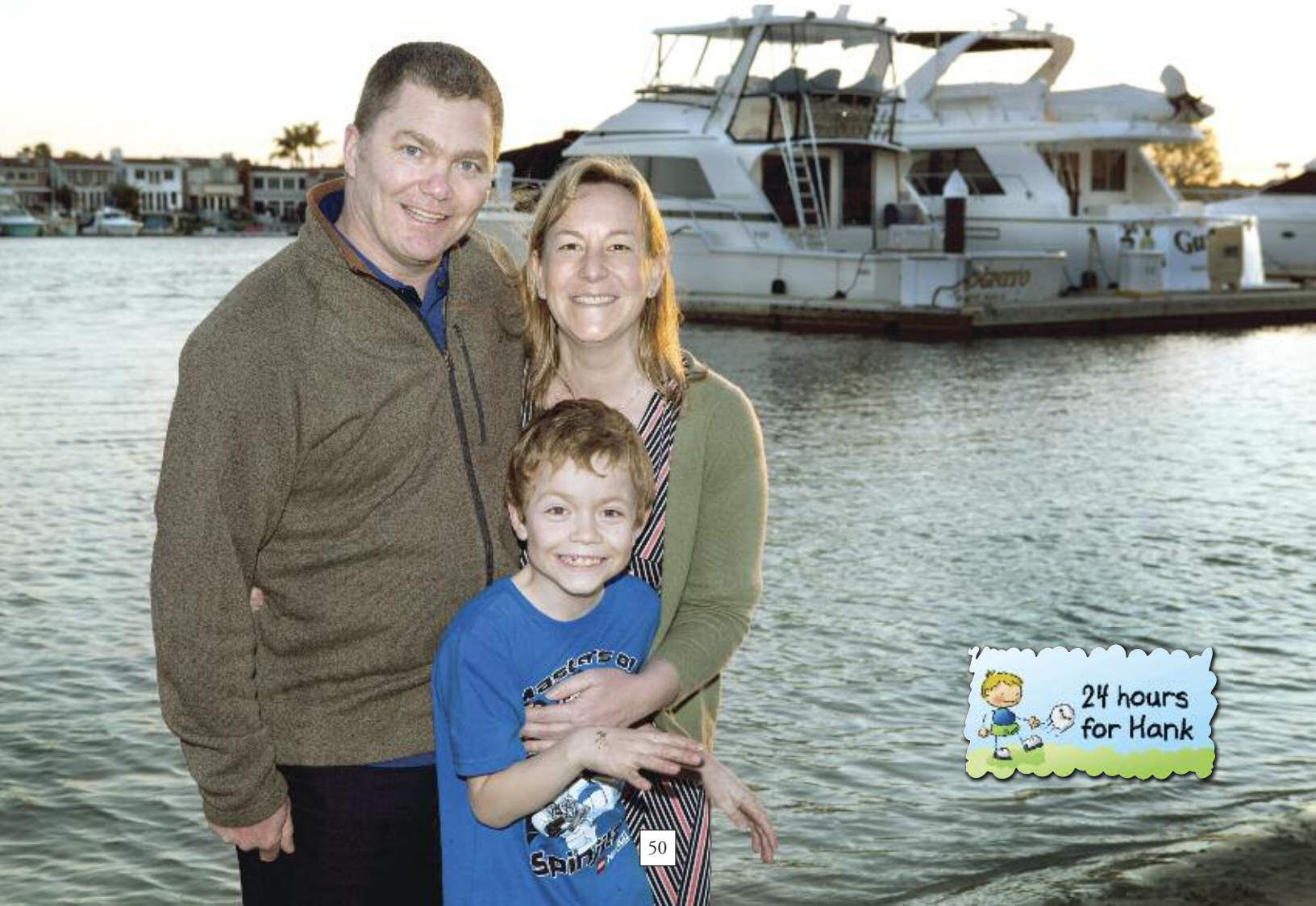
Henry had a great summer of camping and participating in summer camps. He did have one stint in the hospital with a kidney infection in August. We are still doing further testing around that visit.

Fall brings school and Henry is thriving in second grade. He is keeping up academically and finding his way socially. He also continues therapy in school and privately weekly.

Henry started ukulele lessons in September and really enjoys music. He is getting stronger, more coordinated, gaining endurance and confidence.

Thank you to everyone who supports our quest for a cure for cystinosis. No act of kindness, no matter how small, is ever wasted.

With love,
The Sturgis Family
Sandpoint, Idaho



Left to right: John Hatcher, Landy Hauck, Marty Stitsel, Brent Swank, Fred Colby, Jenny Wood, Not Pictured Whit Whitman and Brandon Peterson

SANDPOINT HAS HEART

and you'll find that heart all over our community!

We have had an amazing summer of support for 24 Hours for Hank. Our friends and neighbors have done some really creative fundraising projects.

- In June, **a team of eight bike riders and several support people** from Sandpoint, Idaho, rode from Oceanside, California, to Annapolis, Maryland, in the Race Across America raising awareness for cystinosis, and money for cystinosis research! The team finished the 3,020 mile ride in seven days and 10 hours. (See article at right)
- Also in June, **13-year-old Claire Bennett** opened a boat cleaning service. With more than 20 boats in the neighborhood marina Claire stayed very busy. She then donated 10 percent of her proceeds to 24 Hours for Hank.

- **Nine-year-old Lilly Davis** grew and sold tomato plant starts and donated the proceeds to 24 Hours for Hank.
- We've added three new members to the 24 Hours for Hank Board of Directors. **Kristin Souers** from Spokane, Washington; **Brent Otter** from Bentonville, Arkansas; and **Doug Cameron** from Sandpoint, Idaho, have all been longtime supporters of the foundation. We look forward to leveraging their "24 Hour" enthusiasm and special talents!
- We were also fortunate to receive a huge gift from **Israel Karasek,** who spent many hours redesigning our eight-year-old website. With his help, it's now a first-rate portal to all our activities and we're extremely proud of it.

Unlike other famous races, like the Tour de France, RAAM is not a stage race. In RAAM, once the clock starts on the west coast, the clock doesn't stop until each racer reaches the finish line on the east coast. The route is 3,000 miles – 30 percent longer than the Tour de France – touching 14 states and climbing over 100,000 feet. Teams typically cross the country in 6 to 9 days, averaging 350 to over 500 miles per day.

Why Race RAAM? Some might echo George Mallory's sentiment about Mt. Everest, "Because it's there!"

For most racers it is not that simple. Many racers do it to raise money for a charitable cause. That's why Dave Sturgis, Henry's grandfather, is undertaking this grueling task.

My name is Dave Sturgis and in June of 2015 at 70 years old I will be riding my bike in the world's toughest bicycle race to raise awareness and funds to find a cure for my grandson Henry and those who suffer from cystinosis.

My goal is to raise $100,000. To reach our goal our team has planned several events between now and June. We have also set up a crowdrise fundraising page and this is where I need your help.

www.crowdrise.com/24hoursforhank

There are three simple and very effective ways to help.

❶ DONATE

❷ FUNDRAISE for the campaign

❸ SHARE – Spread the word about the campaign with as many people as you can think of.

With your help, life free of cystinosis is within reach. Thank you for supporting our family's race to save Henry.

24 HOURS OF SCHWEITZER
IS BIGGER AND BETTER THAN EVER

This year's event, will take place on March 21–22, 2015. We've kept our traditional *Endurance Category,* where skiers see how many runs they can make in 24 hours, as well as the *Challenge Category* we added last year. Participants, who said this category was extremely motivating, have to complete a challenge each hour in addition to skiing.

This year's theme is SURVIVOR

Can you SURVIVE a challenge every hour for 24 hours, while you ski?

Or can you SURVIVE skiing 24 hours straight non-stop?

Special thanks to our amazing Title Sponsors.

schweitzer MOUNTAIN RESORT IDAHO

SUBARU

Teams are starting to prepare for 24 Hours of Schweitzer and there have already been several fundraisers around the area. In September, Randi Lui, a 24 Hour of Schweitzer veteran put on a Hawaiian Luau at Laughing Dog Brewery – complete with a pig roast and homemade sweet Hawaiian bread – to raise pledges for her team.

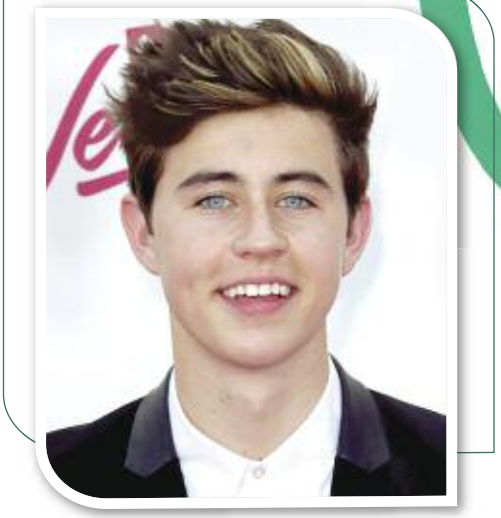
And on October 17, Team All for Hank hosted a premier of *Days of My Life,* a ski movie by Matchstick Productions and Red Bull Media House at the local theater.

Every skier and every volunteer is exhausted by the end of the weekend, but they all realize that they have been part of something very special. They know they have played a critical role in finding a cure for cystinosis – that's why so many of them come back every year.

Henry with superstar skier and 24 Hours for Hank champion fundraiser Matt Gillis

We hope to see you in March 2015. For details, visit www.24hoursforhank.org/events.html

A version of this article originally appeared on CAMBIO.COM on September 19, 2014
http://www.cambio.com/2014/09/19/nash-grier-talks-meeting-fans-giving-back-and-changing-the-wor/



Vine

By Tiffany Taylor

Vine Star Nash Grier Talks About His Cousin Holt, Cystinosis and Changing the World

Vine star Nash Grier has partnered with friends and fellow online sensations **Cameron Dallas, Carter Reynolds** and **Hayes Grier** for a special sweepstakes called **Your Personal Fam Tour.** They want to raise money for their favorite charities.

Here's how it works: No purchase is necessary to enter, but fans can enter by buying a raffle ticket for just one dollar, and the more raffle tickets you buy (the more you donate), the greater your chances of winning.

All of the money raised is being donated to **Hope for Holt, Love is Louder** and the **EVE Foundation**. When the contest ends, the winner and nine of their closest friends will get to spend a day with Nash, Cameron and the rest of the crew. Sounds like a dream come true for one of their lucky fans.

Holt is just the greatest, most joyful bowl of sunshine in the world. You'll never catch the kid without a smile.

We got a chance to chat with Nash about the contest and his newfound fame when he was visiting his home in North Carolina (he was at his little bro's football game when he called us).

Nash chose to donate the sweepstakes proceeds to **Hope for Holt**, a foundation started for his cousin, **Holt Grier**, to raise awareness about a rare disease called cystinosis, as well as support the **Cystinosis Research Foundation** in hopes of finding a cure.

"My cousin Holt (who is now 9 years old) was diagnosed with cystinosis when he was a kid. Cystinosis is a rare disease that destroys all of the body's organs over time. Fortunately, Holt has lived well past what doctors expected and he's doing great right now. He is just the greatest, most joyful bowl of sunshine in the world. You'll never catch the kid without a smile. Holt is a role model for me because of his outlook on life," said Nash. "He's just such a great kid, it's really unfortunate what happened to him, so I just want to bring awareness for his case."

Nash is excited to use his massive social media following to give back, but just as pumped to spend a day with the sweepstakes winner. He told us what he and the guys have in store for the lucky fan.

"Me and Cam argue about this, but I kind of wanted to go to Disneyland, but I've heard, 'Oh you need security,' but Cam's idea was just a dinner and a movie type date," said Nash. "You never really know what's going to end up happening with me, Cam, Carter and Hayes."

Yes, the winners gets to spend a whole day (possibly even go on a date) with the boys. Nash is excited to get the chance to really know some of his biggest fans.

"I love meeting new people. Between all the meet and greets I've done, like MAGCON, DigiFest, we usually don't get to sit and have a conversation with the people that we're meeting and it's really nice to just actually get to know someone who supports you and puts all that time and effort in behind a keyboard," said Nash. "That's really special to me, so I really am looking forward to hanging out with the winners of the sweepstakes."

"Ultimately, I just want to entertain people and make them smile. If I can do that comfortably for the rest of my life, I'll be a happy guy.

I also want to use my following to help people. I want to do something good. I want to change the world and make an impact," said Nash. "I want make a difference, whether that's through Hope for Holt or another charity or another project, I just want to make my mark and change the world."

From Wikipedia, September 25, 2014:
Nash Grier is an American teenager who became nationally known in 2013 for his videos on Vine. As of April 2014 he was the most popular star on Vine.

From https://vine.co/griernash:
Nash Grier: 9.5M followers

Nash with his cousin Holt Grier, who was diagnosed with cystinosis when he was one year old.

2014 BAILEY FEST

Not a day goes by when I walk into my business without being asked by one of my customers, "How's Bailey doing?"

Most have not met Bailey but they know of him, that he is my best friend's son and about his battle with cystinosis. Many of my customers and employees have participated in my fundraising ideas, including raffling off gift certificates and selling Seahawk pint glasses. So, why not have a big fundraising party at the bar?

We held our first annual Bailey Fest 2014 on August 9 and raised more than $5,000. We had music, karaoke, food, prizes and raffles. Our favorite cover band, REWIND, not only rocked the house, but also generously volunteered their time and talent, donating their pay and tips to the cause. Karaoke with KJ Jimmy followed and continued throughout the night. There was singing and dancing all night long!

Cystinosis is not going to take my son from me without a fight. I do not have time to cry anymore, I am a full-time mother on a mission.

JESSICA DEDIO, BAILEY'S MOM

Donate at: www.cystinosisresearch.org/Donate-for-Bailey.

Our friends Roy and Kym Ganzer donated a flat screen TV for the raffle. Friend and liquor sales rep Ben Contreras donated liquor promo items, including t-shirts and a set of Jim Beam bar stools. We also had support from local businesses, including Home Depot, Black Angus, Pielogy, Round Table Pizza, Long Beach Laugh Factory and the Lakewood Chamber of Commerce.

Bailey's mom, Jessica gave a heart-wrenching talk about his life with cystinosis. The crowd roared when she stated, "Cystinosis is not going to take my son from me without a fight. I do not have time to cry anymore, I am a full-time mother on a mission."

When Jessica finished, the crowd thundered,

let's ride.

Thank you to all my employees at the Seahawk Cocktail Lounge, who have helped make my random, crazy fundraising ideas successful.

Finding a cure is near and dear to my heart, not only because of my love for Bailey and Jessica, but because I admire the hard work and passion of CRF families and researchers. I believe our hopes and dreams for a cure will become reality very soon. Until then … let's ride!

Always believe, Tanya Chilcott

By Jessica DeDio, Bailey's mom, Yorba Linda, California

Cocktails and Nails at SeaHawk Lounge

It started when my good friend Lauren Rossner wanted to help raise money for Bailey and his friends with cystinosis. Lauren is a Jamberry Nail consultant. She thought it would be fun to have a girls' cocktail nail party at the Seahawk Cocktail Lounge in Lakewood, California. My best friend and owner of the Seahawk Cocktail Lounge, Tanya Chilcott, thought it was a great idea.

We had the party on July 18 and the night was filled with lots of laugher and "a few drinks," – but mostly it was a night overflowing with love for Bailey and his friends. We sold $880 worth of nails that night and Lauren graciously donated her commission of $264 to the Cystinosis Research Foundation.

Thanks to everyone who made the night a success. And, of course, special thanks and all my love to Lauren, Tanya and Christina.

Second Bailey Believes Yard Sale

At our Second Annual Bailey Believes Yard Sale for a Cure on August 23 and August 30 we raised more than $2,000.

Our wonderful friends, James and Vicki Lape and their family, started the yard sale and I cannot thank them enough. It is very emotional to watch family, friends, friends of friends, co-workers, neighbors and strangers come together to donate and sell items to help find a cure for cystinosis. Thankfully, everyone has lots of fun as well.

Bonnie Paju, mother of cystinosis patient Shannon Paju, and longtime friend of the DeDio family.

This year we received a special donation thanks to our dear friend Dan Dault, who works at Morningside of Fullerton, a retirement home. Morningside was replacing all its furniture and Dan asked if they would donate the old furniture to our yard sale. Morningside happily agreed, giving us more items than ever before for our sale.

Thank you and all my love to everyone who donated items, worked at the yard sale or bought a newly discovered "treasure" there. Special thanks to Morningside and to Dan, Laurie and Brandan Dault. We are blessed to have all of you in our lives.

Bailey Believes
HIS HOPES, HIS DREAMS AND A CURE

We are honored and humbled by the love and support of our family members and friends who have joined us on our journey to the cure. Because of you we are getting closer to our dream of a cure for cystinosis, and we are forever grateful to you.

If you can't join us at one of our Bailey Believes events, please consider donating online at: www.cystinosisresearch.org/donate-for-bailey

Bailey Believes Dirt Bike Ride for a Cure

As this issue of *Cystinosis Magazine* was going to press, the Third Annual Bailey Believes Dirt Bike Ride for a Cure was taking place in Barstow, California. Bailey has been dreaming of this day for more than a year now. It was his first official ride after his kidney transplant on January 14, 2014.

Watch for the details in the next issue of *Cystinosis Magazine.*

3rd Annual

Help Raise Money for the

CYSTINOSIS RESEARCH FOUNDATION

Lots of Love for Landon Charity Golf Outing

By Lauren Hartz, Landon's mom
Pittsburgh, Pennsylvania

The 3rd Annual Lots of Love for Landon Golf Event was held on June 6, 2014 at the Ponderosa Golf Course in Hookstown, PA. One hundred golfers played in Landon's tournament on that beautiful summer day, helping to raise $16,847, which we proudly donated to the Cystinosis Research Foundation.

Landon was more excited than ever to see all the players who came to his "golf party." He even whispered a "thank you" into the microphone before the golfers paraded in carts to their starting holes. Throughout the day he practiced his swing, drove around to check on things and waved to the golfers as they passed him.

Landon, four years old and his brother Jordan 22 months old.

Chinese Auction of 21 items that included car care baskets, fitness club memberships, an iPod Touch, tickets to a Pittsburgh Pirates game, signed Pittsburgh Steelers memorabilia and more. As golfers arrived they received a door prize ticket that gave them an opportunity to win one of 21 items.

Golfers took a chance at winning the 50/50 raffle and a putting contest. They also had the opportunity to participate in a Skins contest and other skills challenges. Landon has incredible support in our community and it was evident at each hole where signs for our 30 hole sponsors were displayed.

The day ended with dinner and prize announcements, along with an update about the incredible progress Landon has made during the past year – and about all the exciting research that is being supported by the CRF.

Each set of hands makes a difference and nothing can bring us so far down that we cannot rise and move forward.

Throughout the event photos were taken of each group of golfers so they would have a souvenir of the day. The photos were also used to create a video, to the song "Hands" by Jewel, as a reminder that each set of hands makes a difference and that nothing can bring us so far down that we cannot rise and move forward.

Jimmy, Landon, Jordan and I are thankful to Jason Whitfield, Jason Hartz and Brad Hamilton for the months of hard work they put into planning this event and making it a success once again. We are also thankful to all of the wonderful people in our lives who volunteered that day and all the golfers who contributed to a cause that is so important to us. You are all making a difference in Landon's life, and in the lives of all those who are affected by this disease. We are forever grateful.

With Love,
Lauren, Jimmy, Landon and Jordan

By Nicole Manz, Keegan's mom
Morrisville, North Carolina

Brad's speedo challenge for cystinosis

Brad Manz is the rock of our family. He is quiet and low-key, and an all-around good guy who is easy to be with. His love for our children and our family continues to amaze me. Through the past year I have seen so much love and strength come from him. Having him by my side is a blessing.

Keegan our one-year-old son, was in a hospital bed almost a year ago. At times, he was listless and sleepy, and other times, he just laid there and cried. He did not want to be held or touched. Brad was the one person who brought him peace. He would stand at Keegan's bedside for hours and sing to keep him calm. I watched the two of them – overwhelmed and scared by everything that was happening. But Brad just kept singing.

As I do dishes at night, I hear him with Keegan and his brother Shane playing and wrestling. Brad tells them how much he loves them, reads to them, and gives them lots of hugs and kisses. But at other times, tender moments when Brad is holding Keegan in his arms, I see his private worries and concern for our happy little guy.

Brad wanted to do something that would let happiness shine on his baby: he put on his speedo for an ice bucket challenge to help spread awareness about this rare disease.

Brad and I, like many other parents of children with a rare disease, put one foot in front of the other every day. We live a different kind of "normal" that is fueled by love and hope. And we work hard not to let our minds wonder too far into the future. All we have is today. When we almost lost our baby to cystinosis, a veil was lifted. Life looked completely different. Our love for life and our family grew deeper. We hold our kids just a little longer, give a few more kisses each day and never miss an opportunity for a good cuddle.

Brad wanted to do something that would let happiness shine on his baby: he put on his speedo for an ice bucket challenge to help spread awareness about this rare disease. By stepping outside his box, Brad was able to raise $3,500!

Thank you to our family and friends, and even a few strangers, for the support you showed during Brad's Speedo Challenge. With your support we will continue to fund more research for better treatments and a cure.

I can't wait to see what Brad's challenge will be next year!

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TOGETHER WE ARE MAKING A DIFFERENCE

Tina Flerchinger

Standing Tall for Cystinosis

Dr. Greg Flerchinger is Tina's Flerchinger's uncle – and he's a really good guy.

He's also a big supporter of Tina's Hope for a Cure and a creative fundraiser for cystinosis research. (We hear he's also an excellent chiropractor.)

Dr. Flerchinger held a Patient Appreciation Week from August 4 through August 8 for his patients in and around Washington Court House, Ohio. All new patients received an exam and x-rays for a special price of $79. He saw his current patients for $15. (We told you he was a good guy.)

Then Dr. Flerchinger donated all proceeds – $2,000 – to cystinosis research, proving once again that we can all help, in our own way, on the journey to the cure.

Annissa and Braelee Bogan set up a lemonade stand at their grandparent's campground to raise money for their friend Landon Hartz and the Cystinosis Research Foundation.

Then Annissa celebrated her birthday by inviting her friends to a party and asked them to donate to the Cystinosis Research Foundation in honor of Landon rather than buying her a birthday present. They raised $100, which they donated to CRF in Landon's honor.

Landon Hartz Halloween

On Saturday, November 1, 2014, just as this issue of *Cystinosis Magazine* was going to press, the Hartz family was holding its 4th Annual Lots of Love for Landon Halloween Fundraiser. Watch for details and pictures in our next issue.

Rockin' on the River for a Cure

The Lewis-Clark community in Idaho, where Tina Flerchinger and her family live, really knows how to party … and how to create a boatload of goodwill while they're doing it.

On July 19, thousands of party-goers from the Lewis Clark Valley attended the annual Rockin' on the River summer concert in Clarkston, Washington. Three national bands – Tantric, Filter and Fuel – entertained the large crowds who came out to take in a little sun, while they enjoyed some great food and music – and to help some folks in need at the same time.

Rockin' on the River raised $20,000. Tina's Hope for a Cure, which received $500, was one of 26 nonprofits to benefit from the event.

Tina and the entire cystinosis community would like to thank the Rockin' on the River Committee for their generosity, and for reminding us that raising money can be a whole lot of fun.

Hearts for Hadley Lemonade

Our family has an amazing support network! Our good friends, Jacqui and Tyler Porter and their three kids, Olivia, Jude and Cici raised $625 for Hearts for Hadley and the Cystinosis Research Foundation by hosting a lemonade stand on August 24.

This is the fifth year the Porter kids have held a lemonade stand to raise money for charity, and it was their most profitable. Their thoughtful and generous family wanted to do their part to support Hearts for Hadley and coordinated the most amazing lemonade stand you've ever seen!

Our family joined forces with them and helped serve lemonade and home-made treats. We met new friends and had the opportunity to explain cystinosis and share information about the disease and our Hearts for Hadley benefit.

Despite being stung by a wasp when the stand opened, Hadley had a great time and enjoyed playing with new and old friends. We even met a dog named, Valentine, who has a black heart on his fur. We decided he should be the Hearts for Hadley mascot!

We are so thankful for the support from our Boise community and the Porter family!

TRADITIONAL JEWELERS MORE COMMITTED TO CRF THAN EVER

Damon and Michele Gross, Michael and Shereen Pollak

Traditional Jewelers in Fashion Island has long been one of CRF's biggest supporters. They recently found a new way to show their support.

Friends of the Cystinosis Research Foundation were invited to a special VIP red carpet, grand opening party for the new and better-than-ever Traditional Jewelers on Wednesday, September 3, 2014. As one of Orange County's most high-profile jewelers, the event, hosted by Traditional Jewelers owners Michael and Shereen Pollak, promised to be quite a soiree. With flutes of champagne in nearly every hand, plates of delectable hors d'oeuvres and great entertainment, guests were not disappointed.

Best of all, Traditional Jewelers and its generous owners donated nearly $14,000 to CRF from the night's proceeds.

TRADITIONAL Jewelers

Andrew's nephrologist Dr. Julian Midgley; Karen McCullagh; and celebrity golfer Jamie Sadlowski, two-time world long drive champion, at the awards dinner.

The Third Annual Fore Fathers Memorial Golf Tournament was held September 13 in honor of four fathers who passed away in their 60's from heart-related diseases. The tournament was held at the Boulder Creek Golf Course in Landon, Alberta, Canada.

Congratulations and thank you to Karen McCullagh and her family for hosting the event in honor of Karen and Don's son Andrew Cunningham. They raised $53,000, which will be shared between the Heart & Stroke Foundation, CRF, which will receive $16,466, and Sick Kids-Cure Cystinosis Fund, which will receive $11,250.

To be part of next year's tournament contact Karen McCullagh at kcm_consulting@msn.com

Hey Cystinosis, Try & Stop Me!

Cystinosis is something that we must contend with every day, whether we feel like it or not – whether we want to or not. It's something we do on our own terms and on our own schedules.

My son, Chandler Moore, chooses to deal with it in way that I find absolutely amazing. Like so many others with cystinosis, he takes his medications, does his eye drops, and bravely lets us give him his daily growth hormone shot. But Chandler says, "I'll do what is required, but I'm making cystinosis deal with me!" – and that's exactly what he does. I have never seen him let cystinosis stop him from doing anything.

This summer, I watched as he joined our local Little League baseball team. He only missed one practice – to attend a cystinosis gala in New Jersey – and he didn't miss a single game. There were days when I thought he should back off because he was experiencing severe leg pain from running, but he said,"No." His performance during the season earned him a spot in the All-Star game, where he again gave his customary 100 percent.

Throughout the summer he worked in our garden and took care of our chickens so he could sell vegetables and fresh eggs to our neighbors. Then he donated his earnings to cystinosis research.

Now he's the manager of our local Pop Warner football team, attending every practice and every game so far. During practices he does all the stretching exercises and sprints with his teammates. During games he runs up and down the sidelines cheering the team on and running water out to the huddles. After the games he often volunteers in the concession stand.

He created his special ***Hey Cystinosis*** bracelet for two reasons: To raise money for cystinosis research, and to develop a warrior spirit in everyone who wears one. **So far Chandler's bracelets have raised $504.**

Cystinosis certainly impacts his life, but Chandler has made cystinosis follow him for many miles and through many adventures. He once told me that cystinosis can either let go, or he would drag it with him. Either way he is going to do exactly what he wants to do. I think the bracelet says it all. **Hey Cystinosis, Try & Stop Me!**

Clinton Moore, Georgetown, Delaware

Shop til You Drop

and raise money for cystinosis research while you do it.

Traci Gendron, new CRF board member, enjoys shopping and over the past few years she has obtained quite the collection of clothing and accessories. Traci wanted to assist her son, Tanner Edwards in his efforts to raise money for cystinosis research and decided to invite friends over to shop from her closet of "gently used and never-worn clothing."

Tanner also designed a special cystinosis tee shirt and conducted his own sales.

Together, Traci and Tanner have raised nearly $4,000 for cystinosis, proving that many hands make lite work and many handbags can make a difference.

To learn more about Traci's *Shop til You Drop* visit: https://www.facebook.com/pages/Clothes-for-a-Cystinosis-Cure/332915810189688

See a photo of Tanner, his mom and his stepfather on page 66.

Family and friends of 10-year-old Caleb Gowan united in *Caleb's Cause* to raise funds for CRF and cystinosis research.

- Dr. Jana Riley-Kraulik, Caleb's mom and her husband Nathan continued to share information about cystinosis with their community.
- Carol Riley, Caleb's grandmother, organized a Tupperware party, sending emails and letters to friends and neighbors to let them know how they could help *Caleb's Cause.*
- Jeremy Gowan, Caleb's dad, persuaded his employer, EIDE Hyundai Motors of North Dakota, to select *Caleb's Cause* and CRF as the recipients of its community services donations for the dealership's casual Fridays.

***Caleb's Cause* and its supporters have raised more than $5,000 for cystinosis research.**

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You've Got Cash!

Hello Jenna and Patrick's Foundation of Hope.

This email confirms that you have received a donation of $1,000 USD from Aunick Lund

We received a wonderful donation from my dear friend and former roommate from Boise, Aunick Lund, and her family. I am from Idaho, and am blessed to say, there are many people from my life there who are a big part of the success of Jenna & Patrick's Foundation of Hope.

I am so grateful to the "many hands who make light work," who hail from the great state of Idaho –- and who knew me long before Jenna and Patrick came on the scene. Lund, Zenner, Johnson, Gotsch, Stringfield, Ford, Lodge, Kimmel, Hamilton, Porter, Shuff, Gasseling, Hall, and of course my family, the Batts ... we thank all of you for your love and loyal support.

Love,
Teresa Batt-Partington
Jenna and Patrick's mom

Teresa and Aunick

it takes a village

WITH LOTS OF ACTIVITIES

February 2015
Gabbie Strauss Fundraiser
CARE (Cystinosis Awareness & Research Effort)
trevors@cystinosis.ca

Saturday, February 7, 2015
Chance for Chase Event
Chase Chodakowsky
www.cystinosisresearch.org/chance-chase

March 21–22, 2015
24 Hours of Schweitzer
Henry Sturgis
Schweitzer Mountain Resort, Sandpoint, Idaho
www.24hoursforhank.org/events/

Friday, March 27, 2015
Jenna & Patrick's Foundation of Hope
Swing Golf Tourney
www.jennaandpatrick.org

Saturday, April 4, 2015
Liv-A-Little Easter Egg Hunt
Olivia Little
Ontario, Canada
Erin Little (519) 832-5188

Saturday, April 11, 2015
Mary Head
Washington
Melissa Head at mhead997@gmail.com

Saturday, May 16, 2015
Tina's Hope for a Cure
Lewiston, Idaho
Denice Flerchinger at mdflerch@gmail.com

Sunday, September 20, 2015
Morgan Peachman
Bob-O-Link Golf Course
Avon, Ohio
www.cystinosisresearch.org/mulligans-fore-morgan

April 16 – April 18, 2015
CRF Day of Hope
Family Conference
Newport Beach, CA
Information: Nancy Stack
nstack@cystinosisresearch.org

Monday, October 19, 2015
Eighth Annual Natalie's Wish
Fore a Cure Golf Tournament
Pelican Hill Golf Course
Newport Beach, CA
Information: Zoe Solsby at zsolsby@cystinosisresearch.org

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NEW CYSTINOSIS RESEARCH FOUNDATION TRUSTEES

The Cystinosis Research Foundation is proud to announce that four new members have been elected to its Board of Trustees. Traci and Tom Gendron, Stephen Jenkins, and Erin Little all have a long history of commitment to CRF and the cystinosis community. We have asked each of them to answer a few questions to help you get to know them.

TRACI AND TOM GENDRON

Mother & stepfather of 26-year-old Tanner Edwards who has cystinosis
Fort Collins, Colorado

Please tell us a little about yourselves.

Traci: I worked as a hairstylist for 25 years, owning my own salon for 11. I also was a board member and volunteer for Crossroads Safehouse, a domestic abuse shelter in Fort Collins, Colorado, where Tom and I live. We also enjoy sharing time in Denver and the mountains.

Tom: I am chairman and CEO of Woodward, Inc. I have been with Woodward for 24 years and have held a variety of jobs across the company. I have a BS in Engineering Physics from the University of Illinois and an MBA from Rockford University. I'm on the boards of several non-profit organizations that are focused on improving the health of our community.

Why are you part of the cystinosis community?

Because Traci's 26-year-old son, Tanner has cystinosis.

Why are you passionate about CRF?

We met Nancy and Jeff Stack a little over two years ago. We were impressed by their passion and drive to find a cure. The amount of funding that CRF has provided for research has given us tremendous hope, and we would like to help find a cure for all the cystinosis families.

What motivates you as a CRF board trustee?

Traci: I want to share information about cystinosis with families and potential donors, and to help CRF raise funds for research.

Tom: I am committed to supporting CRF in its quest to find a cure for cystinosis.

What strengths do you bring to CRF and its mission to find a cure for cystinosis?

Traci: I have a passion for families living with cystinosis. We are both driven to help find a cure.

Tom: I bring experience in governance and operation of public and non-profit organizations, developing and implementing strategies, developing people in their roles, and managing and overseeing the financial health of an organization.

Where do you see CRF five years from now?

Five years from now CRF will have been the catalyst for successful stem cell treatments and will have supported a time when children can be cured of cystinosis.

If you had a wish or a hope what would it be?

To have found a cure for cystinosis, more tolerable medicine for our children, an easier treatment for their eyes, and a day when families will live free of cystinosis.

On October 16, Traci donated a kidney to Tanner.

We are happy to report that Tanner and Traci are doing well.

Photo by Lars Wanberg

STEPHEN JENKINS

Stephen & his wife Ashton are the parents of two-year-old Samuel and five-year-old Lars, who both have cystinosis
Salt Lake City, Utah

Please tell us about yourself.

I live in Salt Lake City, Utah with my wife, Ashton, and my two boys, five-year-old Samuel and two-year-old Lars; our dog, Macey; and our hamster, Akela. I graduated from Brigham Young University with a degree in biology and then attended the University of Utah School of Medicine, where I graduated in May 2014. I am now a first-year-resident physician at the University of Utah Department of Internal Medicine. I work at the University Hospital, Veterans Affairs Medical Center and Intermountain Medical Center.

During college I took two years off to serve a mission for the LDS Church in Donetsk, Ukraine. During medical school I worked in a metabolism lab and studied mechanisms of autophagy in heart muscle cells. I also started a free clinic run by medical students for the homeless in Salt Lake City and was editor-in-chief for the University of Utah Health Sciences Humanities Journal, *Rubor.*

I love hiking, reading, watching movies and spending as much time as possible with my family.

Why are you part of the cystinosis community?

I am part of the cystinosis community because my sons, Samuel and Lars, both have cystinosis. Sam was diagnosed in 2010 around his first birthday. He was lucky to participate in the Procysbi® clinical trial as a young child with a gastric tube. Lars was born in 2012 and diagnosed one month after birth. He is still taking Cystagon®. We are super excited that both boys are swallowing pills now!

Why are you passionate about CRF?

I am passionate about CRF because it has given my family and me tremendous hope for the future of our boys. We were devastated when Sam was diagnosed, and the members of CRF reached out to us and shared their vision.

We attended the Day of Hope Family Conference and learned about the cutting-edge research that the CRF is funding to develop better treatments and to find a cure. When I heard Dr. Cherqui talk about autologous stem cell transplants, I couldn't wait to tell everyone I know. We met other families and watched our children play together. We shared stories, hopes, dreams, worries and fear, and we forged friendships that will last forever. CRF is our family.

What motivates you as a CRF trustee?

My motivation as a CRF trustee is watching my boys deal with cystinosis every day. They are strong and resilient and incredible boys, but I know that the clock is ticking, and that the odds are stacked against them. I want to do everything I can to change those odds.

What strengths do you bring to CRF and its mission to find a cure for cystinosis?

My greatest strength on the CRF Board is my enthusiasm for research and my background in science and medicine, which gives me a unique insight into the quality and relevance of the research CRF is funding. CRF is fortunate to have experts on the Scientific Review Board, who evaluate all research proposals and approves projects for funding. I want to share the amazing things researchers are working on and to make it understandable to people in the cystinosis community. I also want to be an ambassador for CRF's message of hope to all cystinosis families.

Where do you see CRF five years from now?

In five years, I think that there will be a trial for autologous stem cell transplants, the cysteamine nanowafer for corneal cystinosis will be FDA-approved, and people with cystinosis will be walking around with a cysteamine patch instead of taking dozens of pills every day. I hope there will be a bone marrow transplantation from a matched sibling for the currently approved trial. New scientists will join the CRF community to do research on muscle wasting, cardiovascular and neurologic complications, and other quality of life issues.

If you had a wish or a prayer what would it be?

My wish and prayer is that my sons, Samuel and Lars, and all children and adults with cystinosis will have long, happy, meaningful and healthy lives. We will find a cure!

Photo by Ashley Lauersdorf • www.lauersdorfphotography.com

ERIN LITTLE

Erin & her husband Chad are the parents of five-year-old Olivia, who has cystinosis, and 19 month old Harper
Port Elgin, Ontario, Canada

Tell us about your yourself.

I am from Wisconsin, but now live in Port Elgin, Ontario. My husband, Chad and I met while attending the University of Marian in Fond du Lac, Wisconsin, where I earned a BA in psychology with an emphasis in child development. Ontario has been our home for eight years. Before Olivia was born, I taught at a Waldorf-inspired private school. After having Olivia, I decided to remain a stay-at-home mom, but I missed being around other children so I now offer what I call a "Home Away From Home" for other kids – in other words, day care. I spend my days chasing little ones, caring for Olivia and crafting up a storm.

Why are you passionate about CRF?

I had never heard of a foundation that operates like CRF. All costs are underwritten, no salaries are being paid out of donations and it's run by a mother of a young woman with cystinosis. It's easy to be passionate about CRF because of the passion that lies within CRF itself and because everyone is so dedicated to beating cystinosis. CRF doesn't expect change, they demand it.

How did you become connected to the cystinosis community?

When Olivia was diagnosed Chad and I decided to keep to ourselves and find our new balance before seeking support from anyone. We connected with the CRF in December of 2011, five months after Olivia's diagnosis, after speaking to Jody Strauss and Nancy Stack. Now, there is no looking back. Our cystinosis community has become our cystinosis family, where people understand our stresses, our worries and our desire for a cure. When we come together at the CRF Day of Hope Family Conference once a year there is an overwhelming feeling of joy and hope for our children. I never thought we would walk into a room and be able to share hugs, smiles and tears with a group of people who were once strangers. We are all different, have different backgrounds and come from different parts of the world but cystinosis brings us together and makes us a family.

What motivates you as a CRF board trustee?

Our daughter Olivia and the four letter word CURE.

What strengths do you bring to CRF and its mission to find a cure for cystinosis?

I believe anything is possible and that we will find a cure for cystinosis. I tell the truth about cystinosis and what it does to our children and what it means to our family. I have found my voice in bringing awareness to this rare disease and I will not stop until we beat it.

Where do you see CRF five years from now?

Out of business but continuing to raise awareness and educate others about cystinosis.

If you had a prayer or a hope what would it be?

I wish for a cure, I pray that those who live with cystinosis will soon be cystinosis free, and I hope that our children remain happy and become healthy.

"Understand and be confident that each of us can make a difference by caring and acting in small as well as big ways." MARIAN WRIGHT EDELMAN

Farewell to a Dear Friend

SARAH SEWELL MELANG

NOVEMBER 30, 1972 – JUNE 27, 2014

Beloved Sarah was born in Seattle, Washington to Tom and Brenda Melang. The youngest sister to Meri and Tommy, she arrived as the Melang family was moving to their new home in Bellevue, where her parent's still reside. Sarah's childhood was filled with the love of family and friends.

She attended Clyde Hill, Chinook and graduated from Bellevue High in 1991. As a little girl, Sarah loved dance, summer camps, family vacations and tennis. She graduated from the University of Washington and was a member of Sigma Kappa Sorority, where she met lifelong friends. She continued her education at the University of California, Irvine in graphic design at the Art Institute of Orange County.

She was a graphic designer and production coordinator at Seattle Cotton Works from 2006 to the present. Sarah loved her coworkers and dear friends with whom she shared many hours, and she was a hardworking and loyal employee. Sarah's talent as an artist brought her happiness in many ways. She painted birdhouses, boxes and canvas pictures, and made picture cards from photos she took of her favorite flowers, tulips.

Sarah, (second from left) with her mother, Brenda; her brother, Tommy and her father, Tom Melang

She was crazy about her condo in Kirkland, which she decorated with flare, and her convertible VW Cabrio. Sarah was quite the "fashionista" and loved to shop at Nordstrom Rack and always knew how to find a bargain. She volunteered at Virginia Mason delivering flowers to patients.

At a young age, Sarah was diagnosed with cystinosis, a rare genetic disease, which became her greatest challenge over her short 41 years. She endured this tough medical challenge all of her life, the medicines, declining health and muscle atrophy, and two kidney transplants. Tom donated his kidney at the end of her junior year of high school, and Brenda donated her kidney 14 years ago this past May.

Our entire family and Sarah are forever grateful to the wonderful care from her favorite Virginia Mason doctors, Dr. Cyrus Cryst and Dr. Steven Kirtland, as well as the compassionate doctors and nurses at Harborview where Sarah fought her final medical battle after a brain aneurism.

Sarah was our family's special little angel, a loyal friend to all, and truly loved all her friends and family. She was an amazing young woman who didn't let her condition stop her from having a rich, independent and meaningful life. We were truly blessed to have her as a role model for all of us, as a daughter, a sister, a friend and an auntie. Her precious life was a true example of living with passion, character and perseverance regardless of the circumstances.

Sarah, our sweet angel, we will love you forever, and may you stay forever young and forever free, and always in our hearts.

The eulogy from the program at the service of remembrance and thanksgiving in Sarah's honor.

SCIENTIFIC REVIEW BOARD

The Scientific Review Board is composed of leading cystinosis scientists and experts from around the world. Members are actively involved in the grant review process, evaluating and analyzing all research proposals submitted and advising the CRF on the scientific merit of each proposal.

SCIENTIFIC REVIEW BOARD

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2015 CALL FOR RESEARCH PROPOSALS

In 2003, Nancy and Jeff Stack established the non-profit Cystinosis Research Foundation (CRF), with the goal of funding cystinosis research to find better treatments and a cure for cystinosis. Since its inception, CRF has raised more than $25.8 million, with every dollar raised going directly to cystinosis research.

CRF will announce its spring 2015 call for research proposals and fellowships in early 2015. Details and guidelines for applications will be available at: www.cystinosisresearch.org/research/for-researchers.

The Cystinosis Research Foundation utilizes a Scientific Review Board (SRB) comprised of leading international experts in the field of cystinosis. (List at left.) The SRB provides independent, objective reviews and recommendations for each research proposal submitted based on the NIH scale of standards. The SRB follows grant review guidelines established by the Cystinosis Research Foundation (CRF) and advises the CRF on the scientific merits of each proposal.

The goal of the Cystinosis Research Foundation is to speed promising cystinosis research toward clinical trials. To that end, CRF prioritizes research that will lead to better treatments and a cure for cystinosis. CRF issues grants for bench, clinical and translational research, with a strong emphasis on translational and clinical research. CRF is interested in supporting new investigators and encourages them to apply either as research fellows or investigators.

In 2010, CRF established the **Cure Cystinosis International Registry (CCIR)** to serve as a hub of information about cystinosis and its complications. Currently CCIR has approximately 500 registrants in 39 countries around the world. The site contains a Professional Research Portal for researchers who register to access and view de-identified, aggregate cystinosis patient information. **(www.cystinosisregistry.org)**

CRF is excited about the future of cystinosis research, and is grateful to its researchers for their interest in the cystinosis community and its children. We look forward to working together to find better treatments and a cure for cystinosis.

PUBLISHED STUDIES BY CRF-FUNDED RESEARCHERS

(Since our Summer 2014 issue)

- "Lysosomal Cross-Correction by Hematopoietic Stem Cell-Derived Macrophages Via Tunneling Nanotubes" – Published September 1, 2014 in *Stem Cells* by Stéphanie Cherqui, PhD, University of California, San Diego.
- An Opinion Paper on Cystinosis – Published August 27, 2014 in the *Nephrology Dialysis Transplantation* by Elena Levtchenko, University of Leuven, Belgium.

This brings the number of studies published by CRF-Funded researchers to 50.

2014 CRF Spring Research Grants Funded • Total: $1,577,874

Ghanashyam Acharya, PhD, Principal Investigator
Baylor College of Medicine, Houston, Texas
Jennifer Simpson, MD, Co-Principal Investigator
University of California, Irvine
"Development of Extended Release Cysteamine Nanowafer"
$276,380 – 2-year grant
(September 1, 2014 – August 31, 2016)

Anand Bachhawat, PhD, Principal Investigator
Indian Institute of Science Education and Research (IISER), Nagar, Punjab, India
"Genetic and Biochemical Studies on the Cystinosin Transporter Using a Novel Genetic Screen"
$82,500 – 2-year grant
(September 1, 2014 – August 31, 2016)

Sergio Catz, PhD, Mentor
Jinzhong Zhang, PhD, Fellow
The Scripps Research Institute, La Jolla, California
"Improvement of Cellular Function Through Chaperone-Mediated Autophagy and Cellular Trafficking in Cystinosis"
$150,000 – 2-year grant
(September 15, 2014 – September 14, 2016)

Pierre J. Courtoy, MD, PhD, Principal Investigator
Héloïse Chevronnay, PhD, Co-Principal Investigator
Christophe Pierreux, PhD, Co-Principal Investigator
de Duve Institute, UCL, Brussels, Belgium
"Testing Endocytosis-Based Injury with Double Megalin/Cystinosin KO Mice and Exploring Stem Cell: Epithelial Connectivity Across Basement Lamina"
$246,272 – 2-year grant
(September 1, 2014 – August 31, 2016)

Alan Davidson, PhD, Principal Investigator
Teresa Holm, PhD, Co-Principal Investigator
The University of Auckland, Grafton, Auckland, New Zealand
"Cystinotic iPCSs: Generation of Proximal Tubule Cells and Role of the Malate-Aspartate Shuttle"
$207,757 – 2-year grant
(September 1, 2014 – August 31, 2016)

Olivier Devuyst, MD, PhD, Mentor
Alessandro Luciani, PhD, Fellow
Institute of Physiology, UZH, Zürich, Switzerland
"Lysosomal Function, Autophagic Clearance and Junctional Integrity in Nephropathic Cystinosis"
$225,000 – 3-year grant
(September 1, 2014 – August 31, 2017)

Francesco Emma, MD, Principal Investigator
Bambino Gesù Children's Hospital, IRCCS, Rome, Italy
"In Vivo and In Vitro Drug Screening and Testing for Nephropathic Cystinosis"
$214,665 – 2-year grant
(September 1, 2014 – August 31, 2016)

Bruno Gasnier, PhD, Mentor
Xavier Leray, PhD Candidate, Fellow
Université Paris Descartes, Neurophotonics Laboratory/ CNRS, Paris, France
"Mechanism and Modulation of Cysteamine Therapy"
$150,000 – 2-year grant
(October 8, 2014 – October 7, 2016)

Interim Grant Award

Doris Trauner, MD, Principal Investigator
University of California, San Diego
"Academic Achievement and Quality of Life in Individuals with Cystinosis"
$25,300 – 2-month extension grant
(December 1, 2014 – January 31, 2015)

CRF 2014 AUTUMN GRANT AWARDS WILL BE ANNOUNCED IN DECEMBER 2014.

Ghanashyam Acharya, PhD, Principal Investigator
Baylor College of Medicine, Houston, Texas
Jennifer Simpson, MD, Co-Principal Investigator
University of California, Irvine
"Development of Extended Release Cysteamine Nanowafer"
$276,380 – 2-year grant (September 1, 2014 – August 31, 2016)

Objective/Rationale: Corneal cystinosis is presently treated with cysteamine eye drops. Hourly administration of the eye drops several times in a day is often required to treat corneal cystinosis, which is very difficult to comply for infants, school going children, and young adults. Due to multiple administrations on a daily basis, patients develop side effects such as excessive tearing, redness, and ocular inflammation. Consequently, compliance and treatment outcome are severely compromised. This research project focuses on the development of an extended release cysteamine nanowafer to treat corneal cystinosis.

Project Description: This research effort aims to develop an extended release cysteamine nanowafer that can release cysteamine for up to a week with negligible side effects. The nanowafer is a tiny disc (5-8 mm diameter) that can be applied on the cornea with a fingertip. The nanowafer will slowly dissolve and fade away at the end of the stipulated drug release time. The nanowafers will be fabricated by electron-beam lithography and the drug will be loaded by microinjection. The efficacy of the cysteamine nanowafer will be evaluated in cystinosine knock out mice by quantifying the total cysteine concentration in the nanowafer treated group and compared with that of an untreated group. A successful outcome of the preclinical studies will provide a strong evidence-based rationale for the translation of nanowafer drug delivery systems to clinical trials in humans for treating corneal cystinosis.

Relevance to the Understanding and/or Treatment of Cystinosis: The presently available treatment for corneal cystinosis is cysteamine eye drops. The eye drops are although effective, require multiple dosings per day and cause serious side effects. The extended release cysteamine-nanowafer can surmount these issues and improve patient compliance with the treatment. Upon successful development, the cysteamine-nanowafer will be a major advancement in the corneal cystinosis treatment.

Anticipated Outcome: Upon successful completion of the project, a clinically translatable cysteamine-nanowafer drug delivery system will be developed.

Anand Bachhawat, PhD, Principal Investigator
Indian Institute of Science Education and Research (IISER), Nagar, Punjab, India
"Genetic and Biochemical Studies on the Cystinosin Transporter Using a Novel Genetic Screen"
$82,500 – 2-year grant (September 1, 2014 – August 31, 2016)

Objective/Rationale: The cystinosin protein (CTNS) is a lysosomal membrane transporter that transports cystine. The current methods used to evaluate the function of CTNS are cumbersome. This has impeded investigations directed toward finding out the functionally critical parts of the protein. We would like to develop a simpler method to functionally evaluate the protein so that we can subject it to detailed genetic/mutational analysis. The new assay would be yeast-based and would allow one to rapidly evaluate and investigate cystinosin function.

Project Description: Efforts would be made to evaluate yeast as a host to functionally evaluate the human cystinosin transporter. CTNS would be expressed in yeast and the function evaluated by a simple and inexpensive plate assay that would allow one to isolate mutants of the protein for functional evaluation. Mutagenizing a protein followed by functional evaluation is the key to understanding protein function. The yeast method would allow one to do such a mutagenesis – both through a random strategy and a site-directed strategy – and quickly evaluate their function. To confirm the validity of the findings, the function of the protein and the mutants would be compared with their function when expressed in the mammalian system. Using this approach the substrate-binding channels and other functionally important domains could be delineated.

Relevance to the Understanding and/or Treatment of Cystinosis: As cystinosis is caused by a defect in CTNS, it is important to have an in-depth understanding of CTNS as it would enable one to understand how the different kinds of mutations (in CTNS) found in cystinosis patients would impact the functioning of the transporter, and the disease manifestation. Different levels of functioning might require different kinds of treatment. This in-depth understanding of CTNS is currently lacking. We hope that the method developed here would greatly accelerate our understanding of the protein and thereby have an impact on the treatment.

Anticipated Outcome: The method developed for functional evaluation of CTNS would facilitate and augment the efforts on describing the critical features of the protein in terms of substrate-binding channels and other functional domains. It is also possible that the method developed could be eventually used as a diagnostic assay in patients for cystinosin protein function.

Sergio Catz, PhD, Mentor • Jinzhong Zhang, PhD, Fellow
The Scripps Research Institute, La Jolla, California
"Improvement of Cellular Function Through Chaperone-Mediated Autophagy and Cellular Trafficking in Cystinosis"
$150,000 – 2-year grant (September 15, 2014 – September 14, 2016)

Objective/Rationale: Mammalian cells contain intracellular compartments intended to degrade macromolecules and then recycle some small components back to the main soluble compartments. These components are then utilized to synthesize new macromolecules. In this way, mammalian cells eliminate unwanted components while saving energy and resources by maintaining a constant supply of essential elements. Degradation takes place in vacuoles denominated lysosomes (Greek roots: luo means "to destroy" and soma means "body.")

In cystinosis, some essential degradative products cannot be recycled and remain in the lysosomes. This induces lysosomal malfunction, lack of resources, accumulation of degradative products, cell malfunction and cell death. We found that one of the specialized lysosomal functions named Chaperone mediated autophagy (CMA) is defective in cystinosis. We propose to study the mechanisms of CMA and to develop strategies to improve cell function in cystinosis.

Project Description: We found that the expression of an important regulatory protein named LAMP2a is decreased in cystinosis. LAMP2a is the only known receptor for chaperone mediated lysosomal degradation. Defective CMA leads to the accumulation of toxic substrates and is involved in the pathogenesis of human diseases including kidney pathologies, neurological disorders, cancer and aging.

We will utilize cystinotic cells from both mouse models and humans with cystinosis to a) study the interplay between CTNS protein and the CMA receptor LAMP2a, b) understand the mechanisms of defective LAMP2a downregulation and mislocalization in cystinotic cells, c) understand the mechanism of defective translocation of substrates for degradation into the lysosomal lumen and d) determine the molecular basis of the regulation of CMA activity by CTNS.

We recently showed that increasing the movement of lysosomes in a cell, facilitates its function by increasing the probability of interaction with regulatory components, in the same way that public transportation enhances the function of a city by facilitating access of citizens to different working areas increasing productivity. We will express trafficking proteins to correct LAMP2a distribution and function. Finally, we will check the hypothesis that the accumulation of degradative products in lysosomes affects LAMP2a function. We will decrease lysosomal overload and study the role of CTNS mutants on the localization and function of LAMP2a and in the process of chaperone-mediated degradation in cystinotic cells.

Relevance to the Understanding and/or Treatment of Cystinosis: Defective CMA is directly linked to human disease, including kidney pathologies, an organ in which CMA is markedly active. Our research is highly relevant because it identifies, in cystinosis, previously unrevealed cellular defects associated with human pathologies. Elucidating the mechanisms that lead to abnormal CMA in cystinosis and determining strategies to rescue this phenotype will lead to a better understanding of the physiopathology of this disease and to novel approaches for the treatment of cystinosis.

Anticipated Outcome: The aim of our study is to discover why cystinotic cells develop CMA defects and how this impairment can contribute to the pathogenesis of cystinosis. Importantly, we will use different approaches aimed at ameliorating these cellular defects and improving cell function. We expect that our approach will lead to a better understanding of the pathogenic events in cystinosis and to the development of new strategies to improve cell function, which is fundamental to define novel treatments for cystinosis.

Pierre J. Courtoy, MD, PhD, Principal Investigator
Héloïse Chevronnay, PhD, Co-Principal Investigator
Christophe Pierreux, PhD, Co-Principal Investigator
de Duve Institute, UCL, Brussels, Belgium

"Testing Endocytosis-Based Injury with Double Megalin/Cystinosin KO Mice and Exploring Stem Cell: Epithelial Connectivity Across Basement Lamina"
$246,272 – 2-year grant (September 1, 2014 – August 31, 2016)

Objective/Rationale: Our investigations aim at better understanding the natural course of cystinosis and mechanisms of correction by hematopoietic stem cells (HSCs) in cystinotic mice (cystinosin KO). We shall (i) test whether apical receptor-mediated endocytosis of ultrafitrated plasma proteins is the key source of lysosomal cystine in kidney proximal tubular cells (PTCs), primarily injured in nephropathic cystinosis; (ii) define dynamics and molecular actors by which HSCs, attracted by injured PTCs, project as tunneling nanotube (TNTs)/invadopodia and cross tubular basement lamina barrier; and (iii) analyse structure of PTCs basement lamina in cystinosin KO and HSC-grafted cystinotic mice.

Project Description: (i)To test the role of apical receptor-mediated endocytosis, we are generating double KO mice that lack cystinosin in all tissues (cystinosin KO) and are engineered to be further defective for apical receptor-mediated endocytosis selectively in kidney by conditional inactivation of the cornerstone endocytic receptor, megalin (megalin KO). Kidney protection in double KO mice will be evaluated by reference to single cystinosin KO and single megalin KO mice. Lack of protection in other cystinotic organs will serve as control. (ii) Dynamics and molecular machineries involved in TNT/invadopodia formation will be studied by vital multiphoton and high-resolution multiplex immunofluorescence in cystinotic mice engrafted with fluorescent HSCs. We shall focus on HSC polarization toward injured epithelia, cytoskeleton remodeling to support oriented protrusion, molecular motors guiding exocytosis and proteases digesting basement lamina. (iii) Basement lamina structure will be defined by combination of fluorescence and electron microscopy.

Relevance to the Understanding and/or Treatment of Cystinosis: This project thus targets physiopathology of nephropathic cystinosis and mechanisms of stem cell therapy in the kidney.

Anticipated Outcome: These investigations should demonstrate a key role of endocytosis in initiation and progression of nephropathic cystinosis. We also hope to narrow down our understanding of cellular and molecular processes allowing epithelial correction by HSCs, to help optimize the benefit of stem cell therapy.

Alan Davidson, PhD, Principal Investigator • Teresa Holm, PhD, Co-Principal Investigator
The University of Auckland, Grafton, Auckland, New Zealand

"Cystinotic iPCSs: Generation of Proximal Tubule Cells and Role of the Malate-Aspartate Shuttle"
$207,757 – 2-year grant (September 1, 2014 – August 31, 2016)

Objective/Rationale: How cystine accumulation in the proximal tubule cells of the kidney causes renal damage in cystinosis is largely unclear. A major challenge to solving this problem is a lack of good laboratory models of cystinosis. To help overcome this, we have generated cystinotic stem cells (called induced pluripotent stem cells; iPSCs) that can form any cell type in the body. The objectives of this proposal are to convert cystinotic iPSCs into proximal tubule cells and use these cells to (1) identify differences between normal and diseased cells and (2) explore whether the malate-aspartate shuttle (a biochemical pathway involved in energy production) plays a role in cystinosis.

Project Description: Normal and cystinotic iPSCs will be matured into proximal tubule cells using a method we have developed. How well these cells resemble 'natural' proximal tubule cells will be determined by a 'molecular fingerprinting' approach and functional testing. This analysis will validate the usefulness of iPSC-derived kidney cells and also identify informative cystinosis-specific differences that may lead to new therapeutic targets. The levels of amino acids such aspartate and other metabolites will be examined in cystinotic cells and the therapeutic potential of these factors explored.

Relevance to the Understanding and/or Treatment of Cystinosis: Existing laboratory models of cystinosis do not recapitulate all the defects seen in patients. Thus, there is a need for new sources of cystinotic cells to study. Our project will pioneer the use of iPSC-derived proximal tubule cells as a new tool to investigate the cause of kidney failure in cystinosis. Our analysis of amino acid levels and other metabolites may uncover new ways to treat cystinosis.

Anticipated Outcome: Differences between normal and cystinotic proximal tubule cells will be identified and supplementation of cystinotic cells with metabolites found to be depleted may help correct the cellular defects associated with cystinosis.

Olivier Devuyst, MD, PhD, Mentor • Alessandro Luciani, PhD, Fellow

Institute of Physiology, UZH, Zürich, Switzerland

"Lysosomal Function, Autophagic Clearance and Junctional Integrity in Nephropathic Cystinosis"

$225,000 – 3-year grant (September 1, 2014 – August 31, 2017)

Objective/Rationale: Nephropathic cystinosis is characterized by a generalized dysfunction of the proximal tubule that progresses, if untreated, to end-stage renal disease. By using a *Ctns* mouse model, we demonstrated that the loss of cystinosin function in proximal tubule cells triggers an abnormal transcription program with defects in the endolysosomal pathway leading to the urinary loss of specific ligands, before structural damage or renal failure. These abnormalities raise the question of the mechanism(s) linking lysosomal accumulation of cystine to tubular cell dysfunction associated with nephropathic cystinosis.

Project Description: The overall goal of this project is to take advantage of a detailed characterization of Ctns mouse in vivo, combined to cutting-edge cell biology approaches applied on primary cultures of proximal tubule cells to analyze the role of lysosomal dysfunction as a major pathogenic event in the early stage of cystinosis. The specific aims include: (i) to characterize the progressive "identity crisis" and dysfunction of the lysosomal network; (ii) to evaluate the lysosomal clearance of autophagic cargoes (e.g. autophagosome membrane LC3-II, ubiquitinated proteins and dysfunctional mitochondria); (iii) to investigate how the decline of autophagic-lysosomal clearance affects the integrity of the junctional complex proteins and leads to an abnormal transcriptional program causing proliferation and apical dedifferentiation of the proximal tubule cells.

Relevance to the Understanding and/or Treatment of Cystinosis: Obtaining insights into the role of lysosomal dysfunction in the early chain of events leading to proximal tubule cell dysfunction, before structural damage, should yield new therapeutic targets in order to reverse clinically relevant manifestations of nephropathic cystinosis.

Anticipated Outcome: These translational investigations will address the role of failure of lysosomal network in the early stage of disease, and may point to cellular pathways that could be targeted (or monitored) before any structural, irreversible damage of the kidney. The mechanisms identified in early cystinosis may also be relevant for other forms of tubular disorders, helping us to better understand the link between proximal tubule dysfunction and renal disease progression.

Francesco Emma, MD, Principal Investigator

Bambino Gesù Children's Hospital, IRCCS, Rome, Italy

"In Vivo and In Vitro Drug Screening and Testing for Nephropathic Cystinosis"

$214,665 – 2-year grant (September 1, 2014 – August 31, 2016)

Objective/Rationale: Despite very significant improvements over the past decades, treatment for cystinosis remains sub-optimal and new therapies are needed. To this end, we have begun screening a drug library for compounds that can decrease cystine content or the rate of cell death (apoptosis) in cystinosis cells.

Project Description: In this project, we will test directly in cystinotic mice the benefits of one drug that was identified in our previous screening. This drug will be tested in alternative or in combination with cysteamine. In addition, we will use newly identified characteristics of cystinotic cells to search for additional drugs that may be beneficial to patients.

Relevance to the Understanding and/or Treatment of Cystinosis: This application is aimed at improving treatment of nephropathic cystinosis by testing directly in animal models one drug that has the potential of being useful in treating this disease and at searching additional candidate molecules.

Anticipated Outcome: Should the results of these tests be positive, they may lead to directly testing new therapies in human subjects.

Bruno Gasnier, PhD, Mentor • Xavier Leray, PhD Candidate, Fellow
Université Paris Descartes, Neurophotonics Laboratory/CNRS, Paris, France
"Mechanism and Modulation of Cysteamine Therapy"
$150,000 – 2-year grant (October 8, 2014 – October 7, 2016)

Objective/Rationale: Cystinosis is caused by accumulation of the amino acid cystine in an intracellular organelle, the lysosome. Cysteamine, the main treatment of cystinosis, rescues this defect by converting cystine into a new compound that exits lysosomes through the newly discovered protein PQLC2. This role of PQLC2 in cysteamine therapy was established using a cellular model of cystinosis. We now aim to examine this process at the organismal level using a mouse model of the disease. Our project will also test whether the activity of PQLC2 can be modulated to potentiate cysteamine therapy.

Project Description: Drugs susceptible to modulate PQLC2 will be tested on purified lysosomes and in cellular models of cystinosis. The activity of PQLC2 will be measured using selective radiolabelled substrates. Alternatively, we will use an analytical technique (mass spectrometry) to follow the buildup and decay of the reaction product formed by cystine and cysteamine.

Cystinosis is caused by mutation of the CTNS gene. To assess the role of PQLC2 in the whole animal, we will breed mice defective for the PQLC2 gene with the current mouse model of cystinosis, which is defective for the CTNS gene. This will generate mice carrying mutations in both genes. These mice will be characterized at biochemical, histological and behavioral levels and compared with the current model. In a second step, the two models will be treated with cysteamine and subjected to biochemical and histological analyses in various organs.

Relevance to the Understanding and/or Treatment of Cystinosis: The novel mouse model should tell us whether PQLC2 is involved in cysteamine therapy for all organs and could provide a molecular basis for differences in cystine depletion efficacy. The genetic inactivation of PQLC2 may also exacerbate the severity of cystinosis in the absence of treatment according to preliminary data obtained with cellular models. The search for PQLC2 modulators aims to improve cysteamine therapy.

Anticipated Outcome: As a result of our study, we expect to arrive at a molecular understanding for inter-organ and, possibly, inter-individual differences in the response to cysteamine therapy. Furthermore, the identification of PQLC2 modulators could open the way towards more effective pharmacological treatments of cystinosis.

Interim Grant Award

Doris Trauner, MD, Principal Investigator
University of California, San Diego
"Academic Achievement and Quality of Life in Individuals with Cystinosis"
$25,300 – 2-month extension grant (December 1, 2014 – January 31, 2015)

The work to be completed during this time includes two specific aims: (1) To complete data analysis and manuscript completion for the adolescent quality of life study then submit the paper for publication and (2) To conduct data analysis on the PROMIS study, write the manuscript and submit it for journal publication.

Cystinosis Research Foundation

We are indebted to everyone who serves on a Cystinosis Research Foundation Board for their leadership, guidance and commitment to helping our children.

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MISSION

The mission of the Cystinosis Research Foundation is to find better treatments and a cure for cystinosis by supporting bench, clinical and translational research. Since 2003, CRF has raised $25.8 million for cystinosis research in an effort to find a cure.

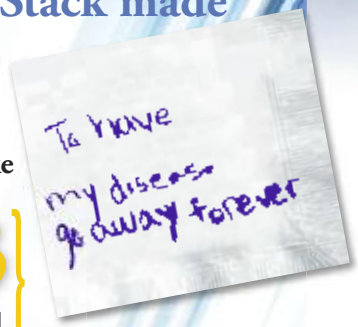
EDUCATION

The CRF is dedicated to educating the medical and public communities about cystinosis to ensure early diagnosis and proper treatment.

CYSTINOSIS RESEARCH FOUNDATION

The Wish that Changed the World

On the eve of her 12th birthday, **Natalie Stack made a wish** no child should ever have to make



In **2003** CRF was Founded

50 articles resulting from **CRF-funded** research have been **published**

DURING THE FOLLOWING **11 YEARS** AND WITH SUPPORT FROM ITS MANY FRIENDS, CRF HAS RAISED **$25.8 MILLION** TO BRING NATALIE'S WISH CLOSER TO REALITY

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The Power of ONE

Thank you to everyone who has traveled with us on the journey towards a cure. Each of you has made a remarkable difference. We appreciate you more than words can express. Now, we hope you will stay with us to finish what we have so nobly started – ***to find the cure for cystinosis.***

60 RENOWNED **SCIENTISTS** FROM **AROUND** THE **GLOBE** attended the 2014 International Cystinosis Research Symposium

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